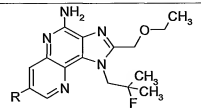
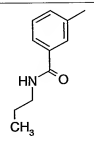
Examples 343 - 350



Example	Reagent	R	Measured Mass (M+H)
	None		396.0825
343	Pyridine-3-boronic acid		395.1991
344	Thiophene-3-boronic acid		400.1602
345	3-Hydroxyphenylboronic acid		410.2020
346	4-(Hydroxymethyl)-phenylboronic acid		424.2136
347	4-Methoxyphenylboronic acid		424.2139
348	3-Chlorophenylboronic acid		428.1655
349	(3-Aminocarbonylphenyl)-boronic acid		437.2093

350	3-(*N*-Propylaminocarbonyl)-phenylboronic acid		479.2554

Examples 351 – 365

Part A

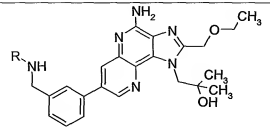
The method described in Examples 339 – 342 was used to treat 1-[4-amino-7-bromo-2-(ethoxymethyl)-1*H*-imidazo[4,5-*c*][1,5]naphthyridin-1-yl]-2-methylpropan-2-ol (1.6 g, 4.06 mmol) with (3-aminomethylphenyl)boronic acid hydrochloride (1.3 g, 6.94 mmol), potassium carbonate (3.0 g, 22 mmol), and dichlorobis(triphenylphosphine)palladium(II) (0.128 g, 0.182 mmol) in DME (20 mL) and water (10 mL). The reaction was heated for 15.5 hours. The eluent used for chromatographic purification was 5% to 25% 1 M methanolic ammonia in dichloromethane. Following chromatographic purification 1.19 g of 1-[4-amino-7-[3-(aminomethyl)phenyl]-2-(ethoxymethyl)-1*H*-imidazo[4,5-*c*][1,5]naphthyridin-1-yl]-2-methylpropan-2-ol were obtained as a yellow solid.

Part B

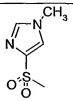
An acid chloride, sulfonyl chloride, or isocyanate (0.11 mmol, 1.1 equivalents) from the table below was added to a test tube containing 1-[4-amino-7-[3-(aminomethyl)phenyl]-2-(ethoxymethyl)-1*H*-imidazo[4,5-*c*][1,5]naphthyridin-1-yl]-2-methylpropan-2-ol (41.7 mg, 0.10 mmol) and *N,N*-diisopropylethylamine (0.034 mL, 0.20 mmol) in *N,N*-dimethylacetamide (DMA) (1 mL). The test tube was capped and vortexed overnight at room temperature. Water (0.100 mL) was added to each test tube, and the solvent was removed by vacuum centrifugation.

The compounds were purified according to the method described in Examples 77 – 127. The table below shows the reagent added to each test tube, the structure of the resulting compound, and the observed accurate mass for the isolated trifluoroacetate salt.

Examples 351 - 365



Example	Reagent	R	Measured Mass (M+H)
351	None	H—	421.2331
352	Acetyl chloride		463.2497
353	Cyclopentanecarbonyl chloride		517.2947
354	Benzoyl chloride		525.2606
355	Cyclohexanecarbonyl chloride		531.3110
356	Nicotinoyl chloride hydrochloride		526.2570
357	Ethanesulfonyl chloride		513.2332
358	Isopropylsulfonyl chloride		527.2480

359	Benzenesulfonyl chloride		561.2324
360	1-Methylimidazole-4-sulfonyl chloride		565.2375
361	2,2,2-Trifluoroethanesulfonyl chloride		567.2000
362	Methyl isocyanate		478.2566
363	Cyclopentyl isocyanate		532.3046
364	Phenyl isocyanate		540.2700
365	4-Morpholinylcarbonyl chloride		534.2824

Examples 366 – 369

Part A

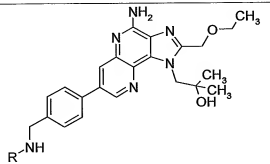
A suspension of 1-[4-amino-7-bromo-2-(ethoxymethyl)-1*H*-imidazo[4,5-*c*][1,5]naphthyridin-1-yl]-2-methylpropan-2-ol (1.6 g, 4.06 mmol), (4-aminomethylphenyl)boronic acid hydrochloride (0.913 g, 4.87 mmol), potassium carbonate (2.5 g, 18 mmol), dichlorobis(triphenylphosphine)palladium(II) (0.028 g, 0.041 mmol), DME (15 mL), and water (7 mL) was stirred under a nitrogen atmosphere and then

heated at 110 °C for 18 hours and allowed to cool to room temperature. An analysis by LC/MS indicated the reaction was incomplete, and additional dichlorobis(triphenylphosphine)palladium(II) (0.050 g) was added. Heating was continued for another six hours, but the reaction did not progress. Additional (4-aminomethylphenyl)boronic acid hydrochloride (0.400 g), potassium carbonate (0.500 g) and dichlorobis(triphenylphosphine)palladium(II) (0.050 g) were added. The reaction was heated at 110 °C for six hours, allowed to cool to room temperature, and concentrated under reduced pressure. Chromatographic purification was carried out as described in Examples 351 - 365 to provide 1.13 g of 1-[4-amino-7-[4-(aminomethyl)phenyl]-2-(ethoxymethyl)-1*H*-imidazo[4,5-*c*][1,5]naphthyridin-1-yl]-2-methylpropan-2-ol as a yellow solid.

Part B

The method described in Part B of Examples 351 – 365 was followed using 1-[4-amino-7-[4-(aminomethyl)phenyl]-2-(ethoxymethyl)-1*H*-imidazo[4,5-*c*][1,5]naphthyridin-1-yl]-2-methylpropan-2-ol instead of 1-[4-amino-7-[3-(aminomethyl)phenyl]-2-(ethoxymethyl)-1*H*-imidazo[4,5-*c*][1,5]naphthyridin-1-yl]-2-methylpropan-2-ol. The table below shows the reagent added to each test tube, the structure of the resulting compound, and the observed accurate mass for the isolated trifluoroacetate salt.

Examples 366 - 369

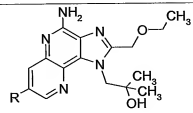


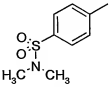
Example	Reagent	R	Measured Mass (M+H)
366	None	H	421.2330
367	Isobutyryl chloride		491.2799
368	Benzoyl chloride		525.2647
369	Isopropylsulfonyl chloride		527.2454

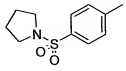
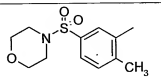
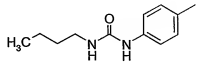
Examples 370 - 378

The methods described in Examples 154 – 194 were followed using 1-[4-amino-7-bromo-2-(ethoxymethyl)-1*H*-imidazo[4,5-*c*][1,5]naphthyridin-1-yl]-2-methylpropan-2-ol (39.2 mg, 0.100 mmol) instead of 1-(4-amino-7-bromo-2-ethyl-1*H*-imidazo[4,5-*c*][1,5]naphthyridin-1-yl)-2-methylpropan-2-ol with the modification that the samples were not diluted in methanol after the initial heating at 80 °C overnight. The table below shows the reagent added to each test tube, the structure of the resulting compound, and the observed accurate mass for the isolated trifluoroacetate salt.

Examples 370 - 378



Example	Reagent	R	Measured Mass (M+H)
370	(2-Methoxymethylphenyl)-boronic acid		436.2349
371	(2-Acetylaminophenyl)-boronic acid		449.2288
372	(2-Trifluoromethylphenyl)-boronic acid		460.1941
373	(2-Methylsulfonylphenyl)-boronic acid		470.1868
374	*N,N*-Dimethyl 4-boronobenzenesulfonamide		499.2109
375	(4-Methanesulfonylaminomethyl phenyl)boronic acid		499.2140

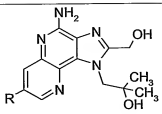
376	*N*-Pyrrolidinyl 4-boronobenzenesulfonamide		525.2261
377	*N*-Morpholinyl 3-borono-4-methylbenzenesulfonamide		555.2371
378	4-(3-Butylureido)phenyl-boronic acid, pinacol ester		506.2886

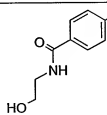
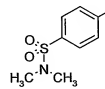
Examples 379 - 388

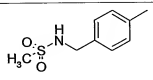
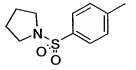
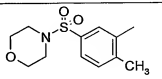
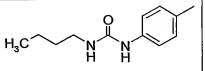
1-[4-Amino-7-bromo-2-(ethoxymethyl)-1*H*-imidazo[4,5-*c*][1,5]naphthyridin-1-yl]-2-methylpropan-2-ol (0.039 g, 0.10 mmol) was added to a test tube. The boronic acid (0.11 mmol) indicated in the table below and *n*-propanol (1.6 mL) were sequentially added. The test tube was purged with nitrogen. Palladium (II) acetate (0.150 mL of a 4 mg/mL solution in toluene, 0.0026 mmol), 2 M aqueous sodium carbonate solution (0.600 mL), deionized water (113 µL), and a solution of 0.15 mol% triphenylphosphine in *n*-propanol (53 µL, 0.0078 mmol) were sequentially added. The test tube was purged with nitrogen, capped, and then heated at 80 °C overnight.

The contents of each test tube were passed through a Waters Oasis Sample Extractions Cartridge MCX (6 cc) according to the procedure described in Examples 4 - 58. The resulting basic solutions were concentrated by vacuum centrifugation. Each sample was subjected to the reaction with boron tribromide described in Examples 128 – 151 using 0.400 mL of boron tribromide solution for each test tube. Each reaction was stirred for six hours at room temperature. After methanol and 6 N hydrochloric acid were added to each tube, the contents were vortexed for 30 minutes, and the volatiles were removed by vacuum centrifugation. The compounds were purified by reversed phase prep HPLC according to the method described in Examples 77 – 127. The table below shows the reagent added to each test tube, the structure of the resulting compound, and the observed accurate mass for the isolated trifluoroacetate salt.

Examples 379 - 388

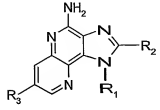


Example	Reagent	R	Measured Mass (M+H)
379	(2-Methoxymethylphenyl)-boronic acid		394.1862
380	(2-Acetylaminophenyl)boronic acid		421.1979
381	(2-Trifluoromethylphenyl)-boronic acid		432.1639
382	(3-Methylsulfonylphenyl)-boronic acid		442.1564
383	[4-(2-Methoxyethylaminocarbonyl)-phenyl]boronic acid		451.2094
384	*N,N*-Dimethyl 4-boronobenzenesulfonamide		471.1804

385	(4-Methanesulfonylamino-methylphenyl)boronic acid		471.1806
386	*N*-Pyrrolidinyl 4-boronobenzenesulfonamide		497.1988
387	*N*-Morpholinyl 3-borono-4-methylbenzenesulfonamide		527.2061
388	4-(3-Butylureido)phenyl-boronic acid, pinacol ester		478.2562

Exemplary Compounds Table

Certain exemplary compounds, including some of those described above in the Examples, have the following Formula (III) wherein R_1, R_2, and R_3 are defined immediately below and in the table. In this table, each row represents one specific compound and a specific embodiment of the invention.



III

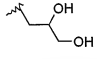
wherein:

R_1 is preferably selected from the following:

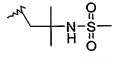
2-hydroxy-2-methylpropyl

2-methylpropyl

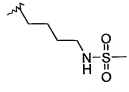
propyl



2,3-dihydroxypropyl



2-methanesulfonylamino-2-methylpropyl
(i.e., 2-methyl-2-[(methylsulfonyl)amino]propyl)



4-methanesulfonylaminobutyl
(i.e., 4-[(methylsulfonyl)amino]butyl)

2-fluoro-2-methylpropyl

R_2 is preferably selected from the following:

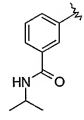
$-CH_3$	$-CH_2CH_3$	$-CH_2CH_2CH_3$	$-CH_2OCH_3$
methyl	ethyl	propyl	methoxymethyl

$-CH_2OCH_2CH_3$	$-CH_2CH_2OCH_3$
ethoxymethyl	2-methoxyethyl

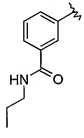
$-CH_2OH$	$-CH_2CH_2OH$
hydroxymethyl	2-hydroxyethyl

R_3 is preferably selected from the following:

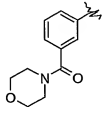
3-pyridyl
(i.e., pyridin-3-yl)



3-[(isopropylamino)carbonyl]phenyl

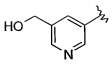


3-[(propylamino)carbonyl]phenyl

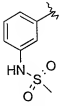


3-(morpholine-4-carbonyl)phenyl
(i.e., 3-(morpholin-4-ylcarbonyl)phenyl)

6-fluoropyridin-3-yl



5-(hydroxymethyl)pyridin-3-yl



3-[(methylsulfonyl)amino]phenyl

R_1	R_2	R_3
2-hydroxy-2-methylpropyl	methyl	pyridin-3-yl
2-hydroxy-2-methylpropyl	methyl	3-[(isopropylamino)carbonyl]phenyl
2-hydroxy-2-methylpropyl	methyl	3-[(propylamino)carbonyl]phenyl
2-hydroxy-2-methylpropyl	methyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-hydroxy-2-methylpropyl	methyl	6-fluoropyridin-3-yl
2-hydroxy-2-methylpropyl	methyl	5-(hydroxymethyl)pyridin-3-yl
2-hydroxy-2-methylpropyl	methyl	3-[(methylsulfonyl)amino]phenyl
2-hydroxy-2-methylpropyl	ethyl	pyridin-3-yl
2-hydroxy-2-methylpropyl	ethyl	3-[(isopropylamino)carbonyl]phenyl
2-hydroxy-2-methylpropyl	ethyl	3-[(propylamino)carbonyl]phenyl
2-hydroxy-2-methylpropyl	ethyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-hydroxy-2-methylpropyl	ethyl	6-fluoropyridin-3-yl
2-hydroxy-2-methylpropyl	ethyl	5-(hydroxymethyl)pyridin-3-yl
2-hydroxy-2-methylpropyl	ethyl	3-[(methylsulfonyl)amino]phenyl
2-hydroxy-2-methylpropyl	propyl	pyridin-3-yl
2-hydroxy-2-methylpropyl	propyl	3-[(isopropylamino)carbonyl]phenyl
2-hydroxy-2-methylpropyl	propyl	3-[(propylamino)carbonyl]phenyl
2-hydroxy-2-methylpropyl	propyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-hydroxy-2-methylpropyl	propyl	6-fluoropyridin-3-yl
2-hydroxy-2-methylpropyl	propyl	5-(hydroxymethyl)pyridin-3-yl
2-hydroxy-2-methylpropyl	propyl	3-[(methylsulfonyl)amino]phenyl
2-hydroxy-2-methylpropyl	methoxymethyl	pyridin-3-yl
2-hydroxy-2-methylpropyl	methoxymethyl	3-[(isopropylamino)carbonyl]phenyl
2-hydroxy-2-methylpropyl	methoxymethyl	3-[(propylamino)carbonyl]phenyl
2-hydroxy-2-methylpropyl	methoxymethyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-hydroxy-2-methylpropyl	methoxymethyl	6-fluoropyridin-3-yl
2-hydroxy-2-methylpropyl	methoxymethyl	5-(hydroxymethyl)pyridin-3-yl

2-hydroxy-2-methylpropyl	methoxymethyl	3-[(methylsulfonyl)amino]phenyl
2-hydroxy-2-methylpropyl	ethoxymethyl	pyridin-3-yl
2-hydroxy-2-methylpropyl	ethoxymethyl	3-[(isopropylamino)carbonyl]phenyl
2-hydroxy-2-methylpropyl	ethoxymethyl	3-[(propylamino)carbonyl]phenyl
2-hydroxy-2-methylpropyl	ethoxymethyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-hydroxy-2-methylpropyl	ethoxymethyl	6-fluoropyridin-3-yl
2-hydroxy-2-methylpropyl	ethoxymethyl	5-(hydroxymethyl)pyridin-3-yl
2-hydroxy-2-methylpropyl	ethoxymethyl	3-[(methylsulfonyl)amino]phenyl
2-hydroxy-2-methylpropyl	2-methoxyethyl	pyridin-3-yl
2-hydroxy-2-methylpropyl	2-methoxyethyl	3-[(isopropylamino)carbonyl]phenyl
2-hydroxy-2-methylpropyl	2-methoxyethyl	3-[(propylamino)carbonyl]phenyl
2-hydroxy-2-methylpropyl	2-methoxyethyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-hydroxy-2-methylpropyl	2-methoxyethyl	6-fluoropyridin-3-yl
2-hydroxy-2-methylpropyl	2-methoxyethyl	5-(hydroxymethyl)pyridin-3-yl
2-hydroxy-2-methylpropyl	2-methoxyethyl	3-[(methylsulfonyl)amino]phenyl
2-hydroxy-2-methylpropyl	hydroxymethyl	pyridin-3-yl
2-hydroxy-2-methylpropyl	hydroxymethyl	3-[(isopropylamino)carbonyl]phenyl
2-hydroxy-2-methylpropyl	hydroxymethyl	3-[(propylamino)carbonyl]phenyl
2-hydroxy-2-methylpropyl	hydroxymethyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-hydroxy-2-methylpropyl	hydroxymethyl	6-fluoropyridin-3-yl
2-hydroxy-2-methylpropyl	hydroxymethyl	5-(hydroxymethyl)pyridin-3-yl
2-hydroxy-2-methylpropyl	hydroxymethyl	3-[(methylsulfonyl)amino]phenyl
2-hydroxy-2-methylpropyl	2-hydroxyethyl	pyridin-3-yl
2-hydroxy-2-methylpropyl	2-hydroxyethyl	3-[(isopropylamino)carbonyl]phenyl
2-hydroxy-2-methylpropyl	2-hydroxyethyl	3-[(propylamino)carbonyl]phenyl
2-hydroxy-2-methylpropyl	2-hydroxyethyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-hydroxy-2-methylpropyl	2-hydroxyethyl	6-fluoropyridin-3-yl
2-hydroxy-2-methylpropyl	2-hydroxyethyl	5-(hydroxymethyl)pyridin-3-yl
2-hydroxy-2-methylpropyl	2-hydroxyethyl	3-[(methylsulfonyl)amino]phenyl
2-methylpropyl	methyl	pyridin-3-yl
2-methylpropyl	methyl	3-[(isopropylamino)carbonyl]phenyl
2-methylpropyl	methyl	3-[(propylamino)carbonyl]phenyl
2-methylpropyl	methyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-methylpropyl	methyl	6-fluoropyridin-3-yl
2-methylpropyl	methyl	5-(hydroxymethyl)pyridin-3-yl
2-methylpropyl	methyl	3-[(methylsulfonyl)amino]phenyl
2-methylpropyl	ethyl	pyridin-3-yl
2-methylpropyl	ethyl	3-[(isopropylamino)carbonyl]phenyl
2-methylpropyl	ethyl	3-[(propylamino)carbonyl]phenyl
2-methylpropyl	ethyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-methylpropyl	ethyl	6-fluoropyridin-3-yl
2-methylpropyl	ethyl	5-(hydroxymethyl)pyridin-3-yl

2-methylpropyl	ethyl	3-[(methylsulfonyl)amino]phenyl
2-methylpropyl	propyl	pyridin-3-yl
2-methylpropyl	propyl	3-[(isopropylamino)carbonyl]phenyl
2-methylpropyl	propyl	3-[(propylamino)carbonyl]phenyl
2-methylpropyl	propyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-methylpropyl	propyl	6-fluoropyridin-3-yl
2-methylpropyl	propyl	5-(hydroxymethyl)pyridin-3-yl
2-methylpropyl	propyl	3-[(methylsulfonyl)amino]phenyl
2-methylpropyl	methoxymethyl	pyridin-3-yl
2-methylpropyl	methoxymethyl	3-[(isopropylamino)carbonyl]phenyl
2-methylpropyl	methoxymethyl	3-[(propylamino)carbonyl]phenyl
2-methylpropyl	methoxymethyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-methylpropyl	methoxymethyl	6-fluoropyridin-3-yl
2-methylpropyl	methoxymethyl	5-(hydroxymethyl)pyridin-3-yl
2-methylpropyl	methoxymethyl	3-[(methylsulfonyl)amino]phenyl
2-methylpropyl	ethoxymethyl	pyridin-3-yl
2-methylpropyl	ethoxymethyl	3-[(isopropylamino)carbonyl]phenyl
2-methylpropyl	ethoxymethyl	3-[(propylamino)carbonyl]phenyl
2-methylpropyl	ethoxymethyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-methylpropyl	ethoxymethyl	6-fluoropyridin-3-yl
2-methylpropyl	ethoxymethyl	5-(hydroxymethyl)pyridin-3-yl
2-methylpropyl	ethoxymethyl	3-[(methylsulfonyl)amino]phenyl
2-methylpropyl	2-methoxyethyl	pyridin-3-yl
2-methylpropyl	2-methoxyethyl	3-[(isopropylamino)carbonyl]phenyl
2-methylpropyl	2-methoxyethyl	3-[(propylamino)carbonyl]phenyl
2-methylpropyl	2-methoxyethyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-methylpropyl	2-methoxyethyl	6-fluoropyridin-3-yl
2-methylpropyl	2-methoxyethyl	5-(hydroxymethyl)pyridin-3-yl
2-methylpropyl	2-methoxyethyl	3-[(methylsulfonyl)amino]phenyl
2-methylpropyl	hydroxymethyl	pyridin-3-yl
2-methylpropyl	hydroxymethyl	3-[(isopropylamino)carbonyl]phenyl
2-methylpropyl	hydroxymethyl	3-[(propylamino)carbonyl]phenyl
2-methylpropyl	hydroxymethyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-methylpropyl	hydroxymethyl	6-fluoropyridin-3-yl
2-methylpropyl	hydroxymethyl	5-(hydroxymethyl)pyridin-3-yl
2-methylpropyl	hydroxymethyl	3-[(methylsulfonyl)amino]phenyl
2-methylpropyl	2-hydroxyethyl	pyridin-3-yl
2-methylpropyl	2-hydroxyethyl	3-[(isopropylamino)carbonyl]phenyl
2-methylpropyl	2-hydroxyethyl	3-[(propylamino)carbonyl]phenyl
2-methylpropyl	2-hydroxyethyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-methylpropyl	2-hydroxyethyl	6-fluoropyridin-3-yl
2-methylpropyl	2-hydroxyethyl	5-(hydroxymethyl)pyridin-3-yl

2-methylpropyl	2-hydroxyethyl	3-[(methylsulfonyl)amino]phenyl
propyl	methyl	pyridin-3-yl
propyl	methyl	3-[(isopropylamino)carbonyl]phenyl
propyl	methyl	3-[(propylamino)carbonyl]phenyl
propyl	methyl	3-(morpholin-4-ylcarbonyl)phenyl)
propyl	methyl	6-fluoropyridin-3-yl
propyl	methyl	5-(hydroxymethyl)pyridin-3-yl
propyl	methyl	3-[(methylsulfonyl)amino]phenyl
propyl	ethyl	pyridin-3-yl
propyl	ethyl	3-[(isopropylamino)carbonyl]phenyl
propyl	ethyl	3-[(propylamino)carbonyl]phenyl
propyl	ethyl	3-(morpholin-4-ylcarbonyl)phenyl)
propyl	ethyl	6-fluoropyridin-3-yl
propyl	ethyl	5-(hydroxymethyl)pyridin-3-yl
propyl	ethyl	3-[(methylsulfonyl)amino]phenyl
propyl	propyl	pyridin-3-yl
propyl	propyl	3-[(isopropylamino)carbonyl]phenyl
propyl	propyl	3-[(propylamino)carbonyl]phenyl
propyl	propyl	3-(morpholin-4-ylcarbonyl)phenyl)
propyl	propyl	6-fluoropyridin-3-yl
propyl	propyl	5-(hydroxymethyl)pyridin-3-yl
propyl	propyl	3-[(methylsulfonyl)amino]phenyl
propyl	methoxymethyl	pyridin-3-yl
propyl	methoxymethyl	3-[(isopropylamino)carbonyl]phenyl
propyl	methoxymethyl	3-[(propylamino)carbonyl]phenyl
propyl	methoxymethyl	3-(morpholin-4-ylcarbonyl)phenyl)
propyl	methoxymethyl	6-fluoropyridin-3-yl
propyl	methoxymethyl	5-(hydroxymethyl)pyridin-3-yl
propyl	methoxymethyl	3-[(methylsulfonyl)amino]phenyl
propyl	ethoxymethyl	pyridin-3-yl
propyl	ethoxymethyl	3-[(isopropylamino)carbonyl]phenyl
propyl	ethoxymethyl	3-[(propylamino)carbonyl]phenyl
propyl	ethoxymethyl	3-(morpholin-4-ylcarbonyl)phenyl)
propyl	ethoxymethyl	6-fluoropyridin-3-yl
propyl	ethoxymethyl	5-(hydroxymethyl)pyridin-3-yl
propyl	ethoxymethyl	3-[(methylsulfonyl)amino]phenyl
propyl	2-methoxyethyl	pyridin-3-yl
propyl	2-methoxyethyl	3-[(isopropylamino)carbonyl]phenyl
propyl	2-methoxyethyl	3-[(propylamino)carbonyl]phenyl
propyl	2-methoxyethyl	3-(morpholin-4-ylcarbonyl)phenyl)
propyl	2-methoxyethyl	6-fluoropyridin-3-yl
propyl	2-methoxyethyl	5-(hydroxymethyl)pyridin-3-yl

propyl	2-methoxyethyl	3-[(methylsulfonyl)amino]phenyl
propyl	hydroxymethyl	pyridin-3-yl
propyl	hydroxymethyl	3-[(isopropylamino)carbonyl]phenyl
propyl	hydroxymethyl	3-[(propylamino)carbonyl]phenyl
propyl	hydroxymethyl	3-(morpholin-4-ylcarbonyl)phenyl)
propyl	hydroxymethyl	6-fluoropyridin-3-yl
propyl	hydroxymethyl	5-(hydroxymethyl)pyridin-3-yl
propyl	hydroxymethyl	3-[(methylsulfonyl)amino]phenyl
propyl	2-hydroxyethyl	pyridin-3-yl
propyl	2-hydroxyethyl	3-[(isopropylamino)carbonyl]phenyl
propyl	2-hydroxyethyl	3-[(propylamino)carbonyl]phenyl
propyl	2-hydroxyethyl	3-(morpholin-4-ylcarbonyl)phenyl)
propyl	2-hydroxyethyl	6-fluoropyridin-3-yl
propyl	2-hydroxyethyl	5-(hydroxymethyl)pyridin-3-yl
propyl	2-hydroxyethyl	3-[(methylsulfonyl)amino]phenyl
2,3-dihydroxypropyl	methyl	pyridin-3-yl
2,3-dihydroxypropyl	methyl	3-[(isopropylamino)carbonyl]phenyl
2,3-dihydroxypropyl	methyl	3-[(propylamino)carbonyl]phenyl
2,3-dihydroxypropyl	methyl	3-(morpholin-4-ylcarbonyl)phenyl)
2,3-dihydroxypropyl	methyl	6-fluoropyridin-3-yl
2,3-dihydroxypropyl	methyl	5-(hydroxymethyl)pyridin-3-yl
2,3-dihydroxypropyl	methyl	3-[(methylsulfonyl)amino]phenyl
2,3-dihydroxypropyl	ethyl	pyridin-3-yl
2,3-dihydroxypropyl	ethyl	3-[(isopropylamino)carbonyl]phenyl
2,3-dihydroxypropyl	ethyl	3-[(propylamino)carbonyl]phenyl
2,3-dihydroxypropyl	ethyl	3-(morpholin-4-ylcarbonyl)phenyl)
2,3-dihydroxypropyl	ethyl	6-fluoropyridin-3-yl
2,3-dihydroxypropyl	ethyl	5-(hydroxymethyl)pyridin-3-yl
2,3-dihydroxypropyl	ethyl	3-[(methylsulfonyl)amino]phenyl
2,3-dihydroxypropyl	propyl	pyridin-3-yl
2,3-dihydroxypropyl	propyl	3-[(isopropylamino)carbonyl]phenyl
2,3-dihydroxypropyl	propyl	3-[(propylamino)carbonyl]phenyl
2,3-dihydroxypropyl	propyl	3-(morpholin-4-ylcarbonyl)phenyl)
2,3-dihydroxypropyl	propyl	6-fluoropyridin-3-yl
2,3-dihydroxypropyl	propyl	5-(hydroxymethyl)pyridin-3-yl
2,3-dihydroxypropyl	propyl	3-[(methylsulfonyl)amino]phenyl
2,3-dihydroxypropyl	methoxymethyl	pyridin-3-yl
2,3-dihydroxypropyl	methoxymethyl	3-[(isopropylamino)carbonyl]phenyl
2,3-dihydroxypropyl	methoxymethyl	3-[(propylamino)carbonyl]phenyl
2,3-dihydroxypropyl	methoxymethyl	3-(morpholin-4-ylcarbonyl)phenyl)
2,3-dihydroxypropyl	methoxymethyl	6-fluoropyridin-3-yl
2,3-dihydroxypropyl	methoxymethyl	5-(hydroxymethyl)pyridin-3-yl

2,3-dihydroxypropyl	methoxymethyl	3-[(methylsulfonyl)amino]phenyl
2,3-dihydroxypropyl	ethoxymethyl	pyridin-3-yl
2,3-dihydroxypropyl	ethoxymethyl	3-[(isopropylamino)carbonyl]phenyl
2,3-dihydroxypropyl	ethoxymethyl	3-[(propylamino)carbonyl]phenyl
2,3-dihydroxypropyl	ethoxymethyl	3-(morpholin-4-ylcarbonyl)phenyl)
2,3-dihydroxypropyl	ethoxymethyl	6-fluoropyridin-3-yl
2,3-dihydroxypropyl	ethoxymethyl	5-(hydroxymethyl)pyridin-3-yl
2,3-dihydroxypropyl	ethoxymethyl	3-[(methylsulfonyl)amino]phenyl
2,3-dihydroxypropyl	2-methoxyethyl	pyridin-3-yl
2,3-dihydroxypropyl	2-methoxyethyl	3-[(isopropylamino)carbonyl]phenyl
2,3-dihydroxypropyl	2-methoxyethyl	3-[(propylamino)carbonyl]phenyl
2,3-dihydroxypropyl	2-methoxyethyl	3-(morpholin-4-ylcarbonyl)phenyl)
2,3-dihydroxypropyl	2-methoxyethyl	6-fluoropyridin-3-yl
2,3-dihydroxypropyl	2-methoxyethyl	5-(hydroxymethyl)pyridin-3-yl
2,3-dihydroxypropyl	2-methoxyethyl	3-[(methylsulfonyl)amino]phenyl
2,3-dihydroxypropyl	hydroxymethyl	pyridin-3-yl
2,3-dihydroxypropyl	hydroxymethyl	3-[(isopropylamino)carbonyl]phenyl
2,3-dihydroxypropyl	hydroxymethyl	3-[(propylamino)carbonyl]phenyl
2,3-dihydroxypropyl	hydroxymethyl	3-(morpholin-4-ylcarbonyl)phenyl)
2,3-dihydroxypropyl	hydroxymethyl	6-fluoropyridin-3-yl
2,3-dihydroxypropyl	hydroxymethyl	5-(hydroxymethyl)pyridin-3-yl
2,3-dihydroxypropyl	hydroxymethyl	3-[(methylsulfonyl)amino]phenyl
2,3-dihydroxypropyl	2-hydroxyethyl	pyridin-3-yl
2,3-dihydroxypropyl	2-hydroxyethyl	3-[(isopropylamino)carbonyl]phenyl
2,3-dihydroxypropyl	2-hydroxyethyl	3-[(propylamino)carbonyl]phenyl
2,3-dihydroxypropyl	2-hydroxyethyl	3-(morpholin-4-ylcarbonyl)phenyl)
2,3-dihydroxypropyl	2-hydroxyethyl	6-fluoropyridin-3-yl
2,3-dihydroxypropyl	2-hydroxyethyl	5-(hydroxymethyl)pyridin-3-yl
2,3-dihydroxypropyl	2-hydroxyethyl	3-[(methylsulfonyl)amino]phenyl
2-methyl-2-[(methylsulfonyl)amino]propyl	methyl	pyridin-3-yl
2-methyl-2-[(methylsulfonyl)amino]propyl	methyl	3-[(isopropylamino)carbonyl]phenyl
2-methyl-2-[(methylsulfonyl)amino]propyl	methyl	3-[(propylamino)carbonyl]phenyl
2-methyl-2-[(methylsulfonyl)amino]propyl	methyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-methyl-2-[(methylsulfonyl)amino]propyl	methyl	6-fluoropyridin-3-yl
2-methyl-2-[(methylsulfonyl)amino]propyl	methyl	5-(hydroxymethyl)pyridin-3-yl
2-methyl-2-[(methylsulfonyl)amino]propyl	methyl	3-[(methylsulfonyl)amino]phenyl

2-methyl-2-[(methylsulfonyl)amino]propyl	ethyl	pyridin-3-yl
2-methyl-2-[(methylsulfonyl)amino]propyl	ethyl	3-[(isopropylamino)carbonyl]phenyl
2-methyl-2-[(methylsulfonyl)amino]propyl	ethyl	3-[(propylamino)carbonyl]phenyl
2-methyl-2-[(methylsulfonyl)amino]propyl	ethyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-methyl-2-[(methylsulfonyl)amino]propyl	ethyl	6-fluoropyridin-3-yl
2-methyl-2-[(methylsulfonyl)amino]propyl	ethyl	5-(hydroxymethyl)pyridin-3-yl
2-methyl-2-[(methylsulfonyl)amino]propyl	ethyl	3-[(methylsulfonyl)amino]phenyl
2-methyl-2-[(methylsulfonyl)amino]propyl	propyl	pyridin-3-yl
2-methyl-2-[(methylsulfonyl)amino]propyl	propyl	3-[(isopropylamino)carbonyl]phenyl
2-methyl-2-[(methylsulfonyl)amino]propyl	propyl	3-[(propylamino)carbonyl]phenyl
2-methyl-2-[(methylsulfonyl)amino]propyl	propyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-methyl-2-[(methylsulfonyl)amino]propyl	propyl	6-fluoropyridin-3-yl
2-methyl-2-[(methylsulfonyl)amino]propyl	propyl	5-(hydroxymethyl)pyridin-3-yl
2-methyl-2-[(methylsulfonyl)amino]propyl	propyl	3-[(methylsulfonyl)amino]phenyl
2-methyl-2-[(methylsulfonyl)amino]propyl	methoxymethyl	pyridin-3-yl
2-methyl-2-[(methylsulfonyl)amino]propyl	methoxymethyl	3-[(isopropylamino)carbonyl]phenyl
2-methyl-2-[(methylsulfonyl)amino]propyl	methoxymethyl	3-[(propylamino)carbonyl]phenyl
2-methyl-2-[(methylsulfonyl)amino]propyl	methoxymethyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-methyl-2-[(methylsulfonyl)amino]propyl	methoxymethyl	6-fluoropyridin-3-yl
2-methyl-2-[(methylsulfonyl)amino]propyl	methoxymethyl	5-(hydroxymethyl)pyridin-3-yl
2-methyl-2-[(methylsulfonyl)amino]propyl	methoxymethyl	3-[(methylsulfonyl)amino]phenyl
2-methyl-2-[(methylsulfonyl)amino]propyl	ethoxymethyl	pyridin-3-yl
2-methyl-2-[(methylsulfonyl)amino]propyl	ethoxymethyl	3-[(isopropylamino)carbonyl]phenyl
2-methyl-2-	ethoxymethyl	3-[(propylamino)carbonyl]phenyl

[(methylsulfonyl)amino]propyl		
2-methyl-2-[(methylsulfonyl)amino]propyl	ethoxymethyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-methyl-2-[(methylsulfonyl)amino]propyl	ethoxymethyl	6-fluoropyridin-3-yl
2-methyl-2-[(methylsulfonyl)amino]propyl	ethoxymethyl	5-(hydroxymethyl)pyridin-3-yl
2-methyl-2-[(methylsulfonyl)amino]propyl	ethoxymethyl	3-[(methylsulfonyl)amino]phenyl
2-methyl-2-[(methylsulfonyl)amino]propyl	2-methoxyethyl	pyridin-3-yl
2-methyl-2-[(methylsulfonyl)amino]propyl	2-methoxyethyl	3-[(isopropylamino)carbonyl]phenyl
2-methyl-2-[(methylsulfonyl)amino]propyl	2-methoxyethyl	3-[(propylamino)carbonyl]phenyl
2-methyl-2-[(methylsulfonyl)amino]propyl	2-methoxyethyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-methyl-2-[(methylsulfonyl)amino]propyl	2-methoxyethyl	6-fluoropyridin-3-yl
2-methyl-2-[(methylsulfonyl)amino]propyl	2-methoxyethyl	5-(hydroxymethyl)pyridin-3-yl
2-methyl-2-[(methylsulfonyl)amino]propyl	2-methoxyethyl	3-[(methylsulfonyl)amino]phenyl
2-methyl-2-[(methylsulfonyl)amino]propyl	hydroxymethyl	pyridin-3-yl
2-methyl-2-[(methylsulfonyl)amino]propyl	hydroxymethyl	3-[(isopropylamino)carbonyl]phenyl
2-methyl-2-[(methylsulfonyl)amino]propyl	hydroxymethyl	3-[(propylamino)carbonyl]phenyl
2-methyl-2-[(methylsulfonyl)amino]propyl	hydroxymethyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-methyl-2-[(methylsulfonyl)amino]propyl	hydroxymethyl	6-fluoropyridin-3-yl
2-methyl-2-[(methylsulfonyl)amino]propyl	hydroxymethyl	5-(hydroxymethyl)pyridin-3-yl
2-methyl-2-[(methylsulfonyl)amino]propyl	hydroxymethyl	3-[(methylsulfonyl)amino]phenyl
2-methyl-2-[(methylsulfonyl)amino]propyl	2-hydroxyethyl	pyridin-3-yl
2-methyl-2-[(methylsulfonyl)amino]propyl	2-hydroxyethyl	3-[(isopropylamino)carbonyl]phenyl
2-methyl-2-[(methylsulfonyl)amino]propyl	2-hydroxyethyl	3-[(propylamino)carbonyl]phenyl
2-methyl-2-[(methylsulfonyl)amino]propyl	2-hydroxyethyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-methyl-2-[(methylsulfonyl)amino]propyl	2-hydroxyethyl	6-fluoropyridin-3-yl

2-methyl-2-[(methylsulfonyl)amino]propyl	2-hydroxyethyl	5-(hydroxymethyl)pyridin-3-yl
2-methyl-2-[(methylsulfonyl)amino]propyl	2-hydroxyethyl	3-[(methylsulfonyl)amino]phenyl
4-[(methylsulfonyl)amino]butyl	methyl	pyridin-3-yl
4-[(methylsulfonyl)amino]butyl	methyl	3-[(isopropylamino)carbonyl]phenyl
4-[(methylsulfonyl)amino]butyl	methyl	3-[(propylamino)carbonyl]phenyl
4-[(methylsulfonyl)amino]butyl	methyl	3-(morpholin-4-ylcarbonyl)phenyl)
4-[(methylsulfonyl)amino]butyl	methyl	6-fluoropyridin-3-yl
4-[(methylsulfonyl)amino]butyl	methyl	5-(hydroxymethyl)pyridin-3-yl
4-[(methylsulfonyl)amino]butyl	methyl	3-[(methylsulfonyl)amino]phenyl
4-[(methylsulfonyl)amino]butyl	ethyl	pyridin-3-yl
4-[(methylsulfonyl)amino]butyl	ethyl	3-[(isopropylamino)carbonyl]phenyl
4-[(methylsulfonyl)amino]butyl	ethyl	3-[(propylamino)carbonyl]phenyl
4-[(methylsulfonyl)amino]butyl	ethyl	3-(morpholin-4-ylcarbonyl)phenyl)
4-[(methylsulfonyl)amino]butyl	ethyl	6-fluoropyridin-3-yl
4-[(methylsulfonyl)amino]butyl	ethyl	5-(hydroxymethyl)pyridin-3-yl
4-[(methylsulfonyl)amino]butyl	ethyl	3-[(methylsulfonyl)amino]phenyl
4-[(methylsulfonyl)amino]butyl	propyl	pyridin-3-yl
4-[(methylsulfonyl)amino]butyl	propyl	3-[(isopropylamino)carbonyl]phenyl
4-[(methylsulfonyl)amino]butyl	propyl	3-[(propylamino)carbonyl]phenyl
4-[(methylsulfonyl)amino]butyl	propyl	3-(morpholin-4-ylcarbonyl)phenyl)
4-[(methylsulfonyl)amino]butyl	propyl	6-fluoropyridin-3-yl
4-[(methylsulfonyl)amino]butyl	propyl	5-(hydroxymethyl)pyridin-3-yl
4-[(methylsulfonyl)amino]butyl	propyl	3-[(methylsulfonyl)amino]phenyl
4-[(methylsulfonyl)amino]butyl	methoxymethyl	pyridin-3-yl
4-[(methylsulfonyl)amino]butyl	methoxymethyl	3-[(isopropylamino)carbonyl]phenyl
4-[(methylsulfonyl)amino]butyl	methoxymethyl	3-[(propylamino)carbonyl]phenyl
4-[(methylsulfonyl)amino]butyl	methoxymethyl	3-(morpholin-4-ylcarbonyl)phenyl)
4-[(methylsulfonyl)amino]butyl	methoxymethyl	6-fluoropyridin-3-yl
4-[(methylsulfonyl)amino]butyl	methoxymethyl	5-(hydroxymethyl)pyridin-3-yl
4-[(methylsulfonyl)amino]butyl	methoxymethyl	3-[(methylsulfonyl)amino]phenyl
4-[(methylsulfonyl)amino]butyl	ethoxymethyl	pyridin-3-yl
4-[(methylsulfonyl)amino]butyl	ethoxymethyl	3-[(isopropylamino)carbonyl]phenyl
4-[(methylsulfonyl)amino]butyl	ethoxymethyl	3-[(propylamino)carbonyl]phenyl
4-[(methylsulfonyl)amino]butyl	ethoxymethyl	3-(morpholin-4-ylcarbonyl)phenyl)
4-[(methylsulfonyl)amino]butyl	ethoxymethyl	6-fluoropyridin-3-yl
4-[(methylsulfonyl)amino]butyl	ethoxymethyl	5-(hydroxymethyl)pyridin-3-yl
4-[(methylsulfonyl)amino]butyl	ethoxymethyl	3-[(methylsulfonyl)amino]phenyl
4-[(methylsulfonyl)amino]butyl	2-methoxyethyl	pyridin-3-yl
4-[(methylsulfonyl)amino]butyl	2-methoxyethyl	3-[(isopropylamino)carbonyl]phenyl
4-[(methylsulfonyl)amino]butyl	2-methoxyethyl	3-[(propylamino)carbonyl]phenyl
4-[(methylsulfonyl)amino]butyl	2-methoxyethyl	3-(morpholin-4-ylcarbonyl)phenyl)

4-[(methylsulfonyl)amino]butyl	2-methoxyethyl	6-fluoropyridin-3-yl
4-[(methylsulfonyl)amino]butyl	2-methoxyethyl	5-(hydroxymethyl)pyridin-3-yl
4-[(methylsulfonyl)amino]butyl	2-methoxyethyl	3-[(methylsulfonyl)amino]phenyl
4-[(methylsulfonyl)amino]butyl	hydroxymethyl	pyridin-3-yl
4-[(methylsulfonyl)amino]butyl	hydroxymethyl	3-[(isopropylamino)carbonyl]phenyl
4-[(methylsulfonyl)amino]butyl	hydroxymethyl	3-[(propylamino)carbonyl]phenyl
4-[(methylsulfonyl)amino]butyl	hydroxymethyl	3-(morpholin-4-ylcarbonyl)phenyl)
4-[(methylsulfonyl)amino]butyl	hydroxymethyl	6-fluoropyridin-3-yl
4-[(methylsulfonyl)amino]butyl	hydroxymethyl	5-(hydroxymethyl)pyridin-3-yl
4-[(methylsulfonyl)amino]butyl	hydroxymethyl	3-[(methylsulfonyl)amino]phenyl
4-[(methylsulfonyl)amino]butyl	2-hydroxyethyl	pyridin-3-yl
4-[(methylsulfonyl)amino]butyl	2-hydroxyethyl	3-[(isopropylamino)carbonyl]phenyl
4-[(methylsulfonyl)amino]butyl	2-hydroxyethyl	3-[(propylamino)carbonyl]phenyl
4-[(methylsulfonyl)amino]butyl	2-hydroxyethyl	3-(morpholin-4-ylcarbonyl)phenyl)
4-[(methylsulfonyl)amino]butyl	2-hydroxyethyl	6-fluoropyridin-3-yl
4-[(methylsulfonyl)amino]butyl	2-hydroxyethyl	5-(hydroxymethyl)pyridin-3-yl
4-[(methylsulfonyl)amino]butyl	2-hydroxyethyl	3-[(methylsulfonyl)amino]phenyl
2-fluoro-2-methylpropyl	methyl	pyridin-3-yl
2-fluoro-2-methylpropyl	methyl	3-[(isopropylamino)carbonyl]phenyl
2-fluoro-2-methylpropyl	methyl	3-[(propylamino)carbonyl]phenyl
2-fluoro-2-methylpropyl	methyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-fluoro-2-methylpropyl	methyl	6-fluoropyridin-3-yl
2-fluoro-2-methylpropyl	methyl	5-(hydroxymethyl)pyridin-3-yl
2-fluoro-2-methylpropyl	methyl	3-[(methylsulfonyl)amino]phenyl
2-fluoro-2-methylpropyl	ethyl	pyridin-3-yl
2-fluoro-2-methylpropyl	ethyl	3-[(isopropylamino)carbonyl]phenyl
2-fluoro-2-methylpropyl	ethyl	3-[(propylamino)carbonyl]phenyl
2-fluoro-2-methylpropyl	ethyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-fluoro-2-methylpropyl	ethyl	6-fluoropyridin-3-yl
2-fluoro-2-methylpropyl	ethyl	5-(hydroxymethyl)pyridin-3-yl
2-fluoro-2-methylpropyl	ethyl	3-[(methylsulfonyl)amino]phenyl
2-fluoro-2-methylpropyl	propyl	pyridin-3-yl
2-fluoro-2-methylpropyl	propyl	3-[(isopropylamino)carbonyl]phenyl
2-fluoro-2-methylpropyl	propyl	3-[(propylamino)carbonyl]phenyl
2-fluoro-2-methylpropyl	propyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-fluoro-2-methylpropyl	propyl	6-fluoropyridin-3-yl
2-fluoro-2-methylpropyl	propyl	5-(hydroxymethyl)pyridin-3-yl
2-fluoro-2-methylpropyl	propyl	3-[(methylsulfonyl)amino]phenyl
2-fluoro-2-methylpropyl	methoxymethyl	pyridin-3-yl
2-fluoro-2-methylpropyl	methoxymethyl	3-[(isopropylamino)carbonyl]phenyl
2-fluoro-2-methylpropyl	methoxymethyl	3-[(propylamino)carbonyl]phenyl
2-fluoro-2-methylpropyl	methoxymethyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-fluoro-2-methylpropyl	methoxymethyl	6-fluoropyridin-3-yl

2-fluoro-2-methylpropyl	methoxymethyl	5-(hydroxymethyl)pyridin-3-yl
2-fluoro-2-methylpropyl	methoxymethyl	3-[(methylsulfonyl)amino]phenyl
2-fluoro-2-methylpropyl	ethoxymethyl	pyridin-3-yl
2-fluoro-2-methylpropyl	ethoxymethyl	3-[(isopropylamino)carbonyl]phenyl
2-fluoro-2-methylpropyl	ethoxymethyl	3-[(propylamino)carbonyl]phenyl
2-fluoro-2-methylpropyl	ethoxymethyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-fluoro-2-methylpropyl	ethoxymethyl	6-fluoropyridin-3-yl
2-fluoro-2-methylpropyl	ethoxymethyl	5-(hydroxymethyl)pyridin-3-yl
2-fluoro-2-methylpropyl	ethoxymethyl	3-[(methylsulfonyl)amino]phenyl
2-fluoro-2-methylpropyl	2-methoxyethyl	pyridin-3-yl
2-fluoro-2-methylpropyl	2-methoxyethyl	3-[(isopropylamino)carbonyl]phenyl
2-fluoro-2-methylpropyl	2-methoxyethyl	3-[(propylamino)carbonyl]phenyl
2-fluoro-2-methylpropyl	2-methoxyethyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-fluoro-2-methylpropyl	2-methoxyethyl	6-fluoropyridin-3-yl
2-fluoro-2-methylpropyl	2-methoxyethyl	5-(hydroxymethyl)pyridin-3-yl
2-fluoro-2-methylpropyl	2-methoxyethyl	3-[(methylsulfonyl)amino]phenyl
2-fluoro-2-methylpropyl	hydroxymethyl	pyridin-3-yl
2-fluoro-2-methylpropyl	hydroxymethyl	3-[(isopropylamino)carbonyl]phenyl
2-fluoro-2-methylpropyl	hydroxymethyl	3-[(propylamino)carbonyl]phenyl
2-fluoro-2-methylpropyl	hydroxymethyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-fluoro-2-methylpropyl	hydroxymethyl	6-fluoropyridin-3-yl
2-fluoro-2-methylpropyl	hydroxymethyl	5-(hydroxymethyl)pyridin-3-yl
2-fluoro-2-methylpropyl	hydroxymethyl	3-[(methylsulfonyl)amino]phenyl
2-fluoro-2-methylpropyl	2-hydroxyethyl	pyridin-3-yl
2-fluoro-2-methylpropyl	2-hydroxyethyl	3-[(isopropylamino)carbonyl]phenyl
2-fluoro-2-methylpropyl	2-hydroxyethyl	3-[(propylamino)carbonyl]phenyl
2-fluoro-2-methylpropyl	2-hydroxyethyl	3-(morpholin-4-ylcarbonyl)phenyl)
2-fluoro-2-methylpropyl	2-hydroxyethyl	6-fluoropyridin-3-yl
2-fluoro-2-methylpropyl	2-hydroxyethyl	5-(hydroxymethyl)pyridin-3-yl

CYTOKINE INDUCTION IN HUMAN CELLS

Compounds of the invention have been found to modulate cytokine biosynthesis by inducing the production of interferon α and/or tumor necrosis factor α in human cells when tested using the method described below.

An in vitro human blood cell system is used to assess cytokine induction. Activity is based on the measurement of interferon (α) and tumor necrosis factor (α) (IFN-α and TNF-α, respectively) secreted into culture media as described by Testerman et. al. in

"Cytokine Induction by the Immunomodulators Imiquimod and S-27609", *Journal of Leukocyte Biology, 58*, 365-372 (September, 1995).

Blood Cell Preparation for Culture

Whole blood from healthy human donors is collected by venipuncture into vacutainer tubes or syringes containing EDTA. Peripheral blood mononuclear cells (PBMC) are separated from whole blood by density gradient centrifugation using HISTOPAQUE-1077 (Sigma, St. Louis, MO) or Ficoll-Paque Plus (Amersham Biosciences Piscataway, NJ). Blood is diluted 1:1 with Dulbecco's Phosphate Buffered Saline (DPBS) or Hank's Balanced Salts Solution (HBSS). Alternately, whole blood is placed in Accuspin (Sigma) or LeucoSep (Greiner Bio-One, Inc., Longwood, FL) centrifuge frit tubes containing density gradient medium. The PBMC layer is collected and washed twice with DPBS or HBSS and re-suspended at 4 x 10^6 cells/mL in RPMI complete. The PBMC suspension is added to 96 well flat bottom sterile tissue culture plates containing an equal volume of RPMI complete media containing test compound.

Compound Preparation

The compounds are solubilized in dimethyl sulfoxide (DMSO). The DMSO concentration should not exceed a final concentration of 1% for addition to the culture wells. The compounds are generally tested at concentrations ranging from 30-0.014 μM. Controls include cell samples with media only, cell samples with DMSO only (no compound), and cell samples with reference compound.

Incubation

The solution of test compound is added at 60 μM to the first well containing RPMI complete and serial 3 fold dilutions are made in the wells. The PBMC suspension is then added to the wells in an equal volume, bringing the test compound concentrations to the desired range (usually 30-0.014 μM). The final concentration of PBMC suspension is 2 x 10^6 cells/mL. The plates are covered with sterile plastic lids, mixed gently and then incubated for 18 to 24 hours at 37°C in a 5% carbon dioxide atmosphere.

Separation

Following incubation the plates are centrifuged for 10 minutes at 1000 rpm (approximately 200 x g) at 4°C. The cell-free culture supernatant is removed and transferred to sterile polypropylene tubes. Samples are maintained at -30 to -70°C until analysis. The samples are analyzed for IFN-α by ELISA and for TNF-α by IGEN/BioVeris Assay.

Interferon (α) and Tumor Necrosis Factor (α) Analysis

IFN-α concentration is determined with a human multi-subtype colorimetric sandwich ELISA (Catalog Number 41105) from PBL Biomedical Laboratories, Piscataway, NJ. Results are expressed in pg/mL.

The TNF-α concentration is determined by ORIGEN M-Series Immunoassay and read on an IGEN M-8 analyzer from BioVeris Corporation, formerly known as IGEN International, Gaithersburg, MD. The immunoassay uses a human TNF-α capture and detection antibody pair (Catalog Numbers AHC3419 and AHC3712) from Biosource International, Camarillo, CA. Results are expressed in pg/mL.

Assay Data and Analysis

In total, the data output of the assay consists of concentration values of TNF-α and IFN-α (y-axis) as a function of compound concentration (x-axis).

Analysis of the data has two steps. First, the greater of the mean DMSO (DMSO control wells) or the experimental background (usually 20 pg/mL for IFN-α and 40 pg/mL for TNF-α) is subtracted from each reading. If any negative values result from background subtraction, the reading is reported as " * ", and is noted as not reliably detectable. In subsequent calculations and statistics, " * ", is treated as a zero. Second, all background subtracted values are multiplied by a single adjustment ratio to decrease experiment to experiment variability. The adjustment ratio is the area of the reference compound in the new experiment divided by the expected area of the reference compound based on the past 61 experiments (unadjusted readings). This results in the scaling of the reading (y-axis) for the new data without changing the shape of the dose-response curve. The reference compound used is 2-[4-amino-2-ethoxymethyl-6,7,8,9-tetrahydro-α,α-dimethyl-1*H*-imidazo[4,5-*c*]quinolin-1-yl]ethanol hydrate (U.S. Patent No. 5,352,784;

Example 91) and the expected area is the sum of the median dose values from the past 61 experiments.

The minimum effective concentration is calculated based on the background-subtracted, reference-adjusted results for a given experiment and compound. The minimum effective concentration (μmolar) is the lowest of the tested compound concentrations that induces a response over a fixed cytokine concentration for the tested cytokine (usually 20 pg/mL for IFN-α and 40 pg/mL for TNF-α). The maximal response is the maximal amount of cytokine (pg/ml) produced in the dose-response.

CYTOKINE INDUCTION IN HUMAN CELLS

(High Throughput Screen)

The CYTOKINE INDUCTION IN HUMAN CELLS test method described above was modified as follows for high throughput screening.

Blood Cell Preparation for Culture

Whole blood from healthy human donors is collected by venipuncture into vacutainer tubes or syringes containing EDTA. Peripheral blood mononuclear cells (PBMC) are separated from whole blood by density gradient centrifugation using HISTOPAQUE-1077 (Sigma, St. Louis, MO) or Ficoll-Paque Plus (Amersham Biosciences Piscataway, NJ). Whole blood is placed in Accuspin (Sigma) or LeucoSep (Greiner Bio-One, Inc., Longwood, FL) centrifuge frit tubes containing density gradient medium. The PBMC layer is collected and washed twice with DPBS or HBSS and re-suspended at 4 x 10^6 cells/mL in RPMI complete (2-fold the final cell density). The PBMC suspension is added to 96-well flat bottom sterile tissue culture plates.

Compound Preparation

The compounds are solubilized in dimethyl sulfoxide (DMSO). The compounds are generally tested at concentrations ranging from 30 - 0.014 μM. Controls include cell samples with media only, cell samples with DMSO only (no compound), and cell samples with a reference compound 2-[4-amino-2-ethoxymethyl-6,7,8,9-tetrahydro-α,α-dimethyl-1H-imidazo[4,5-c]quinolin-1-yl]ethanol hydrate (U.S. Patent No. 5,352,784; Example 91)

on each plate. The solution of test compound is added at 7.5 mM to the first well of a dosing plate and serial 3 fold dilutions are made for the 7 subsequent concentrations in DMSO. RPMI Complete media is then added to the test compound dilutions in order to reach a final compound concentration of 2-fold higher (60 - 0.028 μM) than the final tested concentration range.

Incubation

Compound solution is then added to the wells containing the PBMC suspension bringing the test compound concentrations to the desired range (usually 30 - 0.014 μM) and the DMSO concentration to 0.4 %. The final concentration of PBMC suspension is $2x10^6$ cells/mL. The plates are covered with sterile plastic lids, mixed gently and then incubated for 18 to 24 hours at 37°C in a 5% carbon dioxide atmosphere.

Separation

Following incubation the plates are centrifuged for 10 minutes at 1000 rpm (approximately 200 g) at 4°C. 4-plex Human Panel MSD MULTI-SPOT 96-well plates are pre-coated with the appropriate capture antibodies by MesoScale Discovery, Inc. (MSD, Gaithersburg, MD). The cell-free culture supernatants are removed and transferred to the MSD plates. Fresh samples are typically tested, although they may be maintained at -30 to -70°C until analysis.

Interferon-α and Tumor Necrosis Factor-α Analysis

MSD MULTI-SPOT plates contain within each well capture antibodies for human TNF-α and human IFN-α that have been pre-coated on specific spots. Each well contains four spots: one human TNF-α capture antibody (MSD) spot, one human IFN- α capture antibody (PBL Biomedical Laboratories, Piscataway, NJ) spot, and two inactive bovine serum albumin spots. The human TNF-α capture and detection antibody pair is from MesoScale Discovery. The human IFN-α multi-subtype antibody (PBL Biomedical Laboratories) captures all IFN-α subtypes except IFN-α F (IFNA21). Standards consist of recombinant human TNF-α (R&D Systems, Minneapolis, MN) and IFN-α (PBL Biomedical Laboratories). Samples and separate standards are added at the time of analysis to each MSD plate. Two human IFN-α detection antibodies (Cat. Nos. 21112 & 21100, PBL) are used in a two to one ratio (weight:weight) to each other to determine the

IFN-α concentrations. The cytokine-specific detection antibodies are labeled with the SULFO-TAG reagent (MSD). After adding the SULFO-TAG labeled detection antibodies to the wells, each well's electrochemoluminescent levels are read using MSD's SECTOR HTS READER. Results are expressed in pg/mL upon calculation with known cytokine standards.

Assay Data and Analysis

In total, the data output of the assay consists of concentration values of TNF-α or IFN-α (y-axis) as a function of compound concentration (x-axis).

A plate-wise scaling is performed within a given experiment aimed at reducing plate-to-plate variability associated within the same experiment. First, the greater of the median DMSO (DMSO control wells) or the experimental background (usually 20 pg/mL for IFN-α and 40 pg/mL for TNF-α) is subtracted from each reading. Negative values that may result from background subtraction are set to zero. Each plate within a given experiment has a reference compound that serves as a control. This control is used to calculate a median expected area under the curve across all plates in the assay. A plate-wise scaling factor is calculated for each plate as a ratio of the area of the reference compound on the particular plate to the median expected area for the entire experiment. The data from each plate are then multiplied by the plate-wise scaling factor for all plates. Only data from plates bearing a scaling factor of between 0.5 and 2.0 (for both cytokines IFN-α, TNF-α) are reported. Data from plates with scaling factors outside the above mentioned interval are retested until they bear scaling factors inside the above mentioned interval. The above method produces a scaling of the y-values without altering the shape of the curve. The reference compound used is 2-[4-amino-2-ethoxymethyl-6,7,8,9-tetrahydro-α,α-dimethyl-1*H*-imidazo[4,5-*c*]quinolin-1-yl]ethanol hydrate (U.S. Patent No. 5,352,784; Example 91). The median expected area is the median area across all plates that are part of a given experiment.

A second scaling may also be performed to reduce inter-experiment variability (across multiple experiments). All background-subtracted values are multiplied by a single adjustment ratio to decrease experiment-to-experiment variability. The adjustment ratio is the area of the reference compound in the new experiment divided by the expected area of the reference compound based on an average of previous experiments (unadjusted

readings). This results in the scaling of the reading (y-axis) for the new data without changing the shape of the dose-response curve. The reference compound used is 2-[4-amino-2-ethoxymethyl-6,7,8,9-tetrahydro-α,α-dimethyl-1*H*-imidazo[4,5-*c*]quinolin-1-yl]ethanol hydrate (U.S. Patent No. 5,352,784; Example 91) and the expected area is the sum of the median dose values from an average of previous experiments.

The minimum effective concentration is calculated based on the background-subtracted, reference-adjusted results for a given experiment and compound. The minimum effective concentration (μmolar) is the lowest of the tested compound concentrations that induces a response over a fixed cytokine concentration for the tested cytokine (usually 20 pg/mL for IFN-α and 40 pg/mL for TNF-α). The maximal response is the maximal amount of cytokine (pg/ml) produced in the dose-response.

TNF-α INHIBITION IN MOUSE CELLS

Certain compounds of the invention may modulate cytokine biosynthesis by inhibiting production of tumor necrosis factor α (TNF-α) when tested using the method described below.

The mouse macrophage cell line Raw 264.7 is used to assess the ability of compounds to inhibit tumor necrosis factor-α (TNF-α) production upon stimulation by lipopolysaccharide (LPS).

Single Concentration Assay:

Blood Cell Preparation for Culture

Raw cells (ATCC) are harvested by gentle scraping and then counted. The cell suspension is brought to 3 x 10^5 cells/mL in RPMI with 10 % fetal bovine serum (FBS). Cell suspension (100 μL) is added to 96-well flat bottom sterile tissues culture plates (Becton Dickinson Labware, Lincoln Park, NJ). The final concentration of cells is 3 x 10^4 cells/well. The plates are incubated for 3 hours. Prior to the addition of test compound the medium is replaced with colorless RPMI medium with 3 % FBS.

Compound Preparation

The compounds are solubilized in dimethyl sulfoxide (DMSO). The DMSO concentration should not exceed a final concentration of 1% for addition to the culture wells. Compounds are tested at 5μM. LPS (Lipopolysaccaride from *Salmonella typhimurium*, Sigma-Aldrich) is diluted with colorless RPMI to the EC_{70} concentration as measured by a dose response assay.

Incubation

A solution of test compound (1μl) is added to each well. The plates are mixed on a microtiter plate shaker for 1 minute and then placed in an incubator. Twenty minutes later the solution of LPS (1 μL, EC_{70} concentration ~ 10 ng/ml) is added and the plates are mixed for 1 minute on a shaker. The plates are incubated for 18 to 24 hours at 37 °C in a 5 % carbon dioxide atmosphere.

TNF-α Analysis

Following the incubation the supernatant is removed with a pipet. TNF-α concentration is determined by ELISA using a mouse TNF- α kit (from Biosource International, Camarillo, CA). Results are expressed in pg/mL. TNF-α expression upon LPS stimulation alone is considered a 100% response.

Dose Response Assay:

Blood Cell Preparation for Culture

Raw cells (ATCC) are harvested by gentle scraping and then counted. The cell suspension is brought to 4 x 10^5 cells/mL in RPMI with 10 % FBS. Cell suspension (250 μL) is added to 48-well flat bottom sterile tissues culture plates (Costar, Cambridge, MA). The final concentration of cells is 1 x 10^5 cells/well. The plates are incubated for 3 hours. Prior to the addition of test compound the medium is replaced with colorless RPMI medium with 3 % FBS.

Compound Preparation

The compounds are solubilized in dimethyl sulfoxide (DMSO). The DMSO concentration should not exceed a final concentration of 1% for addition to the culture wells. Compounds are tested at 0.03, 0.1, 0.3, 1, 3, 5 and 10 μM. LPS

(Lipopolysaccaride from *Salmonella typhimurium*, Sigma-Aldrich) is diluted with colorless RPMI to the EC_{70} concentration as measured by dose response assay.

Incubation

A solution of test compound (200 µl) is added to each well. The plates are mixed on a microtiter plate shaker for 1 minute and then placed in an incubator. Twenty minutes later the solution of LPS (200 µL, EC_{70} concentration ~ 10 ng/ml) is added and the plates are mixed for 1 minute on a shaker. The plates are incubated for 18 to 24 hours at 37 °C in a 5 % carbon dioxide atmosphere.

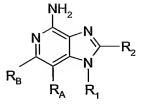
TNF-α Analysis

Following the incubation the supernatant is removed with a pipet. TNF-α concentration is determined by ELISA using a mouse TNF- α kit (from Biosource International, Camarillo, CA). Results are expressed in pg/mL. TNF-α expression upon LPS stimulation alone is considered a 100% response.

The complete disclosures of the patents, patent documents, and publications cited herein are incorporated by reference in their entirety as if each were individually incorporated. Various modifications and alterations to this invention will become apparent to those skilled in the art without departing from the scope and spirit of this invention. It should be understood that this invention is not intended to be unduly limited by the illustrative embodiments and examples set forth herein and that such examples and embodiments are presented by way of example only with the scope of the invention intended to be limited only by the claims set forth herein as follows.

WHAT IS CLAIMED IS:

1. A compound of the Formula I:



I

wherein:

R_A and R_B join to form a fused pyridine ring which is substituted by one R_3 group or substituted by one R_3 group and one R group;

R_1 is selected from the group consisting of:

-R_4,

-X-R_4,

-X-Y-R_4,

-X-Y-X-Y-R_4, and

-X-R_5;

R_2 is selected from the group consisting of:

-R_4,

-X-R_4,

-X-Y-R_4, and

-X-R_5;

R_3 is selected from the group consisting of:

-Z-Ar,

-Z-Ar'-Y-R_4,

-Z-Ar'-X-Y-R_4,

-Z-Ar'-R_5, and

-Z-Ar'-X-R_5;

R is selected from the group consisting of alkyl, alkoxy, chloro, fluoro, hydroxy, and trifluoromethyl;

Ar is selected from the group consisting of aryl and heteroaryl both of which can be unsubstituted or can be substituted by one or more substituents independently selected from the group consisting of alkyl, alkenyl, alkoxy, methylenedioxy, haloalkyl,

haloalkoxy, halogen, nitro, hydroxy, hydroxyalkyl, mercapto, cyano, carboxy, formyl, aryl, aryloxy, arylalkyleneoxy, heteroaryl, heteroaryloxy, heteroarylalkyleneoxy, heterocyclyl, heterocyclylalkylenyl, alkoxyalkylenyl, α-aminocarboxyalkylenyl, amino, aminoalkyl, alkylamino, and dialkylamino;

Ar' is selected from the group consisting of arylene and heteroarylene both of which can be unsubstituted or can be substituted by one or more substituents independently selected from the group consisting of alkyl, alkenyl, alkoxy, haloalkyl, haloalkoxy, halogen, nitro, hydroxy, hydroxyalkyl, mercapto, cyano, carboxy, formyl, aryl, aryloxy, arylalkyleneoxy, heteroaryl, heteroaryloxy, heteroarylalkyleneoxy, heterocyclyl, heterocyclylalkylenyl, amino, alkylamino, and dialkylamino;

X is selected from the group consisting of alkylene, alkenylene, alkynylene, arylene, heteroarylene, and heterocyclylene wherein the alkylene, alkenylene, and alkynylene groups can be optionally interrupted or terminated with arylene, heteroarylene, or heterocyclylene, and optionally interrupted by one or more -O- groups;

Y is selected from the group consisting of:

$-S(O)_{0-2}-$,

$-S(O)_2-N(R_8)-$,

$-C(R_6)-$,

$-C(R_6)-O-$,

$-O-C(R_6)-$,

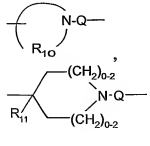
$-O-C(O)-O-$,

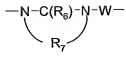
$-N(R_8)-Q-$,

$-C(R_6)-N(R_8)-$,

$-O-C(R_6)-N(R_8)-$,

$-C(R_6)-N(OR_9)-$,

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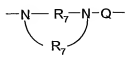
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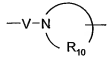
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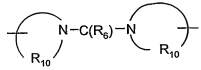
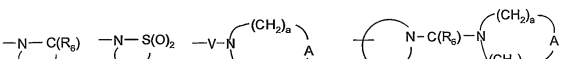

;

Z is selected from the group consisting of a bond, alkylene, alkenylene, and alkynylene;

R_4 is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, arylalkylenyl, aryloxyalkylenyl, alkylarylenyl, heteroaryl, heteroarylalkylenyl, heteroaryloxyalkylenyl, alkylheteroarylenyl, and heterocyclyl wherein the alkyl, alkenyl, alkynyl, aryl, arylalkylenyl, aryloxyalkylenyl, alkylarylenyl, heteroaryl, heteroarylalkylenyl, heteroaryloxyalkylenyl, alkylheteroarylenyl, and heterocyclyl groups can be unsubstituted or substituted by one or more substituents independently selected from the group consisting of alkyl, alkoxy, hydroxyalkyl, haloalkyl, haloalkoxy, halogen, nitro, hydroxy, mercapto, cyano, aryl, aryloxy, arylalkyleneoxy, heteroaryl, heteroaryloxy, heteroarylalkyleneoxy, heterocyclyl, amino, carboxy, alkylamino, dialkylamino, (dialkylamino)alkyleneoxy, and in the case of alkyl, alkenyl, alkynyl, and heterocyclyl, oxo;

R_5 is selected from the group consisting of:


;

R_6 is selected from the group consisting of =O and =S;

R_7 is C_{2-7} alkylene;

R_8 is selected from the group consisting of hydrogen, alkyl, alkoxyalkylenyl, and arylalkylenyl;

R_9 is selected from the group consisting of hydrogen and alkyl;

R_{10} is C_{3-8} alkylene;

R_{11} is selected from the group consisting of fluoro, hydroxy, and alkoxy;

A is selected from the group consisting of -O-, -C(O)-, $-S(O)_{0-2}$-, $-CH_2$-, and $-N(R_4)$-;

Q is selected from the group consisting of a bond, $-C(R_6)$-, $-C(R_6)-C(R_6)$, $-S(O)_2$-, $-C(R_6)-N(R_8)$-W-, $-S(O)_2-N(R_8)$-, $-C(R_6)$-O-, and $-C(R_6)-N(OR_9)$-;

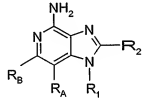
V is selected from the group consisting of $-C(R_6)$-, $-O-C(R_6)$-, $-N(R_8)-C(R_6)$-, and $-S(O)_2$-;

W is selected from the group consisting of a bond, -C(O)-, and $-S(O)_2$-; and

a and b are independently integers from 1 to 6 with the proviso that a + b is ≤ 7;

or a pharmaceutically acceptable salt thereof.

2. A compound of the Formula I:



I

wherein:

R_A and R_B join to form a fused pyridine ring which is substituted by one R_3 group or substituted by one R_3 group and one R group;

R_1 is selected from the group consisting of:

$-R_4$,

$-X-R_4$,

$-X-Y-R_4$,

$-X-Y-X-Y-R_4$, and

$-X-R_5$;

R_2 is selected from the group consisting of:

$-R_4$,

$-X-R_4$,

$-X-Y-R_4$, and

$-X-R_5$;

R_3 is selected from the group consisting of:

-Z-Ar,

-Z-Ar'-Y-R_4,

-Z-Ar'-X-Y-R_4,

-Z-Ar'-R_5, and

-Z-Ar'-X-R_5;

R is selected from the group consisting of alkyl, alkoxy, chloro, fluoro, hydroxy, and trifluoromethyl;

Ar is selected from the group consisting of aryl and heteroaryl both of which can be unsubstituted or can be substituted by one or more substituents independently selected from the group consisting of alkyl, alkenyl, alkoxy, methylenedioxy, haloalkyl, haloalkoxy, halogen, nitro, hydroxy, hydroxyalkyl, mercapto, cyano, carboxy, formyl, aryl, aryloxy, arylalkyleneoxy, heteroaryl, heteroaryloxy, heteroarylalkyleneoxy, heterocyclyl, heterocyclylalkylenyl, amino, aminoalkyl, alkylamino, and dialkylamino;

Ar' is selected from the group consisting of arylene and heteroarylene both of which can be unsubstituted or can be substituted by one or more substituents independently selected from the group consisting of alkyl, alkenyl, alkoxy, haloalkyl, haloalkoxy, halogen, nitro, hydroxy, hydroxyalkyl, mercapto, cyano, carboxy, formyl, aryl, aryloxy, arylalkyleneoxy, heteroaryl, heteroaryloxy, heteroarylalkyleneoxy, heterocyclyl, heterocyclylalkylenyl, amino, alkylamino, and dialkylamino;

X is selected from the group consisting of alkylene, alkenylene, alkynylene, arylene, heteroarylene, and heterocyclylene wherein the alkylene, alkenylene, and alkynylene groups can be optionally interrupted or terminated with arylene, heteroarylene, or heterocyclylene, and optionally interrupted by one or more -O- groups;

Y is selected from the group consisting of:

-$S(O)_{0-2}$-,

-$S(O)_2$-$N(R_8)$-,

-$C(R_6)$-,

-$C(R_6)$-O-,

-O-$C(R_6)$-,

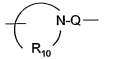
-O-C(O)-O-,

-$N(R_8)$-Q-,

-C(R_6)-N(R_8)-,

-O-C(R_6)-N(R_8)-,

-C(R_6)-N(OR_9)-,



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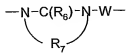

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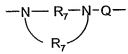

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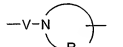

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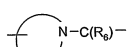
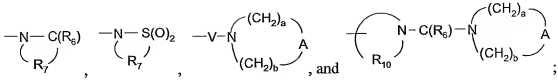


;

Z is selected from the group consisting of a bond, alkylene, alkenylene, and alkynylene;

R_4 is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, arylalkylenyl, aryloxyalkylenyl, alkylarylenyl, heteroaryl, heteroarylalkylenyl, heteroaryloxyalkylenyl, alkylheteroarylenyl, and heterocyclyl wherein the alkyl, alkenyl, alkynyl, aryl, arylalkylenyl, aryloxyalkylenyl, alkylarylenyl, heteroaryl, heteroarylalkylenyl, heteroaryloxyalkylenyl, alkylheteroarylenyl, and heterocyclyl groups can be unsubstituted or substituted by one or more substituents independently selected from the group consisting of alkyl, alkoxy, hydroxyalkyl, haloalkyl, haloalkoxy, halogen, nitro, hydroxy, mercapto, cyano, aryl, aryloxy, arylalkyleneoxy, heteroaryl, heteroaryloxy, heteroarylalkyleneoxy, heterocyclyl, amino, alkylamino, dialkylamino, (dialkylamino)alkyleneoxy, and in the case of alkyl, alkenyl, alkynyl, and heterocyclyl, oxo;

R_5 is selected from the group consisting of:



R_6 is selected from the group consisting of =O and =S;

R_7 is C_{2-7} alkylene;

R_8 is selected from the group consisting of hydrogen, alkyl, alkoxyalkylenyl, and arylalkylenyl;

R_9 is selected from the group consisting of hydrogen and alkyl;

R_{10} is C_{3-8} alkylene;

A is selected from the group consisting of -O-, -C(O)-, $-S(O)_{0-2}$-, $-CH_2$-, and $-N(R_4)$-;

Q is selected from the group consisting of a bond, $-C(R_6)$-, $-C(R_6)-C(R_6)$, $-S(O)_2$-, $-C(R_6)-N(R_8)-W$-, $-S(O)_2-N(R_8)$-, $-C(R_6)-O$-, and $-C(R_6)-N(OR_9)$-;

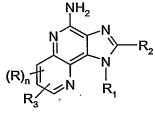
V is selected from the group consisting of $-C(R_6)$-, $-O-C(R_6)$-, $-N(R_8)-C(R_6)$-, and $-S(O)_2$-;

W is selected from the group consisting of a bond, -C(O)-, and $-S(O)_2$-; and

a and b are independently integers from 1 to 6 with the proviso that $a + b$ is ≤ 7;

or a pharmaceutically acceptable salt thereof.

3. A compound of the Formula II:



II

wherein:

n is 0 or 1;

R_1 is selected from the group consisting of:

$-R_4$,

$-X-R_4$,

$-X-Y-R_4$,

-X-Y-X-Y-R_4, and

-X-R_5;

R_2 is selected from the group consisting of:

-R_4,

-X-R_4,

-X-Y-R_4, and

-X-R_5;

R_3 is selected from the group consisting of:

-Z-Ar,

-Z-Ar'-Y-R_4,

-Z-Ar'-X-Y-R_4,

-Z-Ar'-R_5, and

-Z-Ar'-X-R_5;

R is selected from the group consisting of alkyl, alkoxy, chloro, fluoro, hydroxy, and trifluoromethyl;

Ar is selected from the group consisting of aryl and heteroaryl both of which can be unsubstituted or can be substituted by one or more substituents independently selected from the group consisting of alkyl, alkenyl, alkoxy, methylenedioxy, haloalkyl, haloalkoxy, halogen, nitro, hydroxy, hydroxyalkyl, mercapto, cyano, carboxy, formyl, aryl, aryloxy, arylalkyleneoxy, heteroaryl, heteroaryloxy, heteroarylalkyleneoxy, heterocyclyl, heterocyclylalkylenyl, amino, aminoalkyl, alkylamino, and dialkylamino;

Ar' is selected from the group consisting of arylene and heteroarylene both of which can be unsubstituted or can be substituted by one or more substituents independently selected from the group consisting of alkyl, alkenyl, alkoxy, haloalkyl, haloalkoxy, halogen, nitro, hydroxy, hydroxyalkyl, mercapto, cyano, carboxy, formyl, aryl, aryloxy, arylalkyleneoxy, heteroaryl, heteroaryloxy, heteroarylalkyleneoxy, heterocyclyl, heterocyclylalkylenyl, amino, alkylamino, and dialkylamino;

X is selected from the group consisting of alkylene, alkenylene, alkynylene, arylene, heteroarylene, and heterocyclylene wherein the alkylene, alkenylene, and alkynylene groups can be optionally interrupted or terminated with arylene, heteroarylene, or heterocyclylene, and optionally interrupted by one or more -O- groups;

Y is selected from the group consisting of:

-S(O)$_{0-2}$-,

-S(O)$_2$-N(R_8)-,

-C(R_6)-,

-C(R_6)-O-,

-O-C(R_6)-,

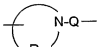
-O-C(O)-O-,

-N(R_8)-Q-,

-C(R_6)-N(R_8)-,

-O-C(R_6)-N(R_8)-,

-C(R_6)-N(OR_9)-,



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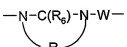

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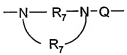

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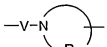

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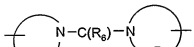


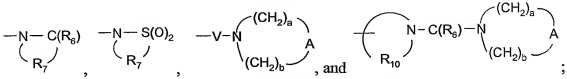
;

Z is selected from the group consisting of a bond, alkylene, alkenylene, and alkynylene;

R_4 is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, arylalkylenyl, aryloxyalkylenyl, alkylarylenyl, heteroaryl, heteroarylalkylenyl, heteroaryloxyalkylenyl, alkylheteroarylenyl, and heterocyclyl wherein the alkyl, alkenyl, alkynyl, aryl, arylalkylenyl, aryloxyalkylenyl, alkylarylenyl, heteroaryl, heteroarylalkylenyl, heteroaryloxyalkylenyl, alkylheteroarylenyl, and heterocyclyl groups can be unsubstituted or substituted by one or more substituents independently selected from the group consisting of alkyl, alkoxy, hydroxyalkyl, haloalkyl, haloalkoxy, halogen,

nitro, hydroxy, mercapto, cyano, aryl, aryloxy, arylalkyleneoxy, heteroaryl, heteroaryloxy, heteroarylalkyleneoxy, heterocyclyl, amino, alkylamino, dialkylamino, (dialkylamino)alkyleneoxy, and in the case of alkyl, alkenyl, alkynyl, and heterocyclyl, oxo;

R_5 is selected from the group consisting of:



R_6 is selected from the group consisting of =O and =S;

R_7 is C_{2-7} alkylene;

R_8 is selected from the group consisting of hydrogen, alkyl, alkoxyalkylenyl, and arylalkylenyl;

R_9 is selected from the group consisting of hydrogen and alkyl;

R_{10} is C_{3-8} alkylene;

A is selected from the group consisting of -O-, -C(O)-, -S(O)$_{0-2}$-, -CH_2-, and -N(R_4)-;

Q is selected from the group consisting of a bond, -C(R_6)-, -C(R_6)-C(R_6), -S(O)$_2$-, -C(R_6)-N(R_8)-W-, -S(O)$_2$-N(R_8)-, -C(R_6)-O-, and -C(R_6)-N(OR_9)-;

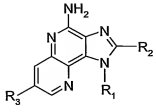
V is selected from the group consisting of -C(R_6)-, -O-C(R_6)-, -N(R_8)-C(R_6)-, and -S(O)$_2$-;

W is selected from the group consisting of a bond, -C(O)-, and –S(O)$_2$-; and

a and b are independently integers from 1 to 6 with the proviso that a + b is ≤ 7;

or a pharmaceutically acceptable salt thereof.

4. A compound of the Formula (III):



III

wherein:

R_1 is selected from the group consisting of:

-R_4,

-X-R_4,

-X-Y-R_4,

-X-Y-X-Y-R_4, and

-X-R_5;

R_2 is selected from the group consisting of:

-R_4,

-X-R_4,

-X-Y-R_4, and

-X-R_5;

R_3 is selected from the group consisting of:

-Z-Ar,

-Z-Ar'-Y-R_4,

-Z-Ar'-X-Y-R_4,

-Z-Ar'-R_5, and

-Z-Ar'-X-R_5;

Ar is selected from the group consisting of aryl and heteroaryl both of which can be unsubstituted or can be substituted by one or more substituents independently selected from the group consisting of alkyl, alkenyl, alkoxy, methylenedioxy, haloalkyl, haloalkoxy, halogen, nitro, hydroxy, hydroxyalkyl, mercapto, cyano, carboxy, formyl, aryl, aryloxy, arylalkyleneoxy, heteroaryl, heteroaryloxy, heteroarylalkyleneoxy, heterocyclyl, heterocyclylalkylenyl, amino, aminoalkyl, alkylamino, and dialkylamino;

Ar' is selected from the group consisting of arylene and heteroarylene both of which can be unsubstituted or can be substituted by one or more substituents independently selected from the group consisting of alkyl, alkenyl, alkoxy, haloalkyl, haloalkoxy, halogen, nitro, hydroxy, hydroxyalkyl, mercapto, cyano, carboxy, formyl, aryl, aryloxy, arylalkyleneoxy, heteroaryl, heteroaryloxy, heteroarylalkyleneoxy, heterocyclyl, heterocyclylalkylenyl, amino, alkylamino, and dialkylamino;

X is selected from the group consisting of alkylene, alkenylene, alkynylene, arylene, heteroarylene, and heterocyclylene wherein the alkylene, alkenylene, and

alkynylene groups can be optionally interrupted or terminated with arylene, heteroarylene, or heterocyclylene, and optionally interrupted by one or more -O- groups;

Y is selected from the group consisting of:

-$S(O)_{0-2}$-,

-$S(O)_2$-$N(R_8)$-,

-$C(R_6)$-,

-$C(R_6)$-O-,

-O-$C(R_6)$-,

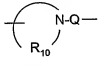
-O-C(O)-O-,

-$N(R_8)$-Q-,

-$C(R_6)$-$N(R_8)$-,

-O-$C(R_6)$-$N(R_8)$-,

-$C(R_6)$-$N(OR_9)$-,



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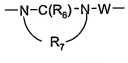

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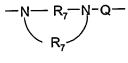

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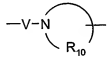

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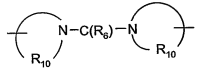


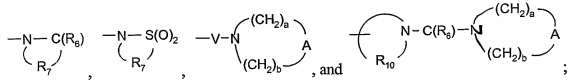
;

Z is selected from the group consisting of a bond, alkylene, alkenylene, and alkynylene;

R_4 is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, arylalkylenyl, aryloxyalkylenyl, alkylarylenyl, heteroaryl, heteroarylalkylenyl, heteroaryloxyalkylenyl, alkylheteroarylenyl, and heterocyclyl wherein the alkyl, alkenyl, alkynyl, aryl, arylalkylenyl, aryloxyalkylenyl, alkylarylenyl, heteroaryl,

heteroarylalkylenyl, heteroaryloxyalkylenyl, alkylheteroarylenyl, and heterocyclyl groups can be unsubstituted or substituted by one or more substituents independently selected from the group consisting of alkyl, alkoxy, hydroxyalkyl, haloalkyl, haloalkoxy, halogen, nitro, hydroxy, mercapto, cyano, aryl, aryloxy, arylalkyleneoxy, heteroaryl, heteroaryloxy, heteroarylalkyleneoxy, heterocyclyl, amino, alkylamino, dialkylamino, (dialkylamino)alkyleneoxy, and in the case of alkyl, alkenyl, alkynyl, and heterocyclyl, oxo;

R_5 is selected from the group consisting of:



;

R_6 is selected from the group consisting of =O and =S;

R_7 is C_{2-7} alkylene;

R_8 is selected from the group consisting of hydrogen, alkyl, alkoxyalkylenyl, and arylalkylenyl;

R_9 is selected from the group consisting of hydrogen and alkyl;

R_{10} is C_{3-8} alkylene;

A is selected from the group consisting of -O-, -C(O)-, $-S(O)_{0-2}-$, $-CH_2-$, and $-N(R_4)-$;

Q is selected from the group consisting of a bond, $-C(R_6)-$, $-C(R_6)-C(R_6)$, $-S(O)_2-$, $-C(R_6)-N(R_8)-W-$, $-S(O)_2-N(R_8)-$, $-C(R_6)-O-$, and $-C(R_6)-N(OR_9)-$;

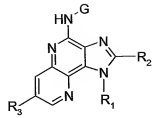
V is selected from the group consisting of $-C(R_6)-$, $-O-C(R_6)-$, $-N(R_8)-C(R_6)-$, and $-S(O)_2-$;

W is selected from the group consisting of a bond, -C(O)-, and $-S(O)_2-$; and

a and b are independently integers from 1 to 6 with the proviso that $a + b$ is ≤ 7;

or a pharmaceutically acceptable salt thereof.

5. A compound of the Formula VII:



VII

wherein:

G is selected from the group consisting of:

-C(O)-R',

α-aminoacyl,

α-aminoacyl-α-aminoacyl,

-C(O)-O-R',

-C(O)-N(R")R',

-C(=NY')-R',

-CH(OH)-C(O)-OY',

-CH(OC_{1-4} alkyl)Y_0,

-CH_2Y_1, and

-$CH(CH_3)Y_1$;

R' and R" are independently selected from the group consisting of C_{1-10} alkyl, C_{3-7} cycloalkyl, and benzyl, each of which may be unsubstituted or substituted by one or more substitutents selected from the group consisting of halogen, hydroxy, nitro, cyano, carboxy, C_{1-6} alkyl, C_{1-4} alkoxy, aryl, heteroaryl, arylC_{1-4} alkylenyl, heteroarylC_{1-4} alkylenyl, haloC_{1-4} alkylenyl, haloC_{1-4} alkoxy, -O-C(O)-CH_3, -C(O)-O-CH_3, -C(O)-NH_2, -O-CH_2-C(O)-NH_2, -NH_2, and –$S(O)_2$-NH_2, with the proviso that R" can also be hydrogen;

α-aminoacyl is an acyl group derived from an amino acid selected from the group consisting of racemic, D-, and L-amino acids;

Y' is selected from the group consisting of hydrogen, C_{1-6} alkyl, and benzyl;

Y_0 is selected from the group consisting of C_{1-6} alkyl, carboxyC_{1-6} alkylenyl, aminoC_{1-4} alkylenyl, mono-*N*-C_{1-6} alkylaminoC_{1-4} alkylenyl, and di-*N*,*N*-C_{1-6} alkylaminoC_{1-4} alkylenyl;

Y_1 is selected from the group consisting of mono-*N*-C_{1-6} alkylamino, di-*N*,*N*-C_{1-6} alkylamino, morpholin-4-yl, piperidin-1-yl, pyrrolidin-1-yl, and 4-C_{1-4} alkylpiperazin-1-yl;

R_1 is selected from the group consisting of:

-R_4,

-X-R_4,

-X-Y-R_4,

-X-Y-X-Y-R_4, and

-X-R_5;

R_2 is selected from the group consisting of:

-R_4,

-X-R_4,

-X-Y-R_4, and

-X-R_5;

R_3 is selected from the group consisting of:

-Z-Ar,

-Z-Ar'-Y-R_4,

-Z-Ar'-X-Y-R_4,

-Z-Ar'-R_5, and

-Z-Ar'-X-R_5;

Ar is selected from the group consisting of aryl and heteroaryl both of which can be unsubstituted or can be substituted by one or more substituents independently selected from the group consisting of alkyl, alkenyl, alkoxy, methylenedioxy, haloalkyl, haloalkoxy, halogen, nitro, hydroxy, hydroxyalkyl, mercapto, cyano, carboxy, formyl, aryl, aryloxy, arylalkyleneoxy, heteroaryl, heteroaryloxy, heteroarylalkyleneoxy, heterocyclyl, heterocyclylalkylenyl, amino, aminoalkyl, alkylamino, and dialkylamino;

Ar' is selected from the group consisting of arylene and heteroarylene both of which can be unsubstituted or can be substituted by one or more substituents independently selected from the group consisting of alkyl, alkenyl, alkoxy, haloalkyl, haloalkoxy, halogen, nitro, hydroxy, hydroxyalkyl, mercapto, cyano, carboxy, formyl, aryl, aryloxy, arylalkyleneoxy, heteroaryl, heteroaryloxy, heteroarylalkyleneoxy, heterocyclyl, heterocyclylalkylenyl, amino, alkylamino, and dialkylamino;

X is selected from the group consisting of alkylene, alkenylene, alkynylene, arylene, heteroarylene, and heterocyclylene wherein the alkylene, alkenylene, and alkynylene groups can be optionally interrupted or terminated with arylene, heteroarylene, or heterocyclylene, and optionally interrupted by one or more -O- groups;

Y is selected from the group consisting of:

$-S(O)_{0-2}-$,

$-S(O)_2-N(R_8)-$,

$-C(R_6)-$,

$-C(R_6)-O-$,

$-O-C(R_6)-$,

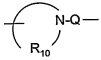
$-O-C(O)-O-$,

$-N(R_8)-Q-$,

$-C(R_6)-N(R_8)-$,

$-O-C(R_6)-N(R_8)-$,

$-C(R_6)-N(OR_9)-$,



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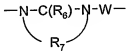

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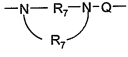

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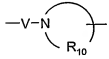

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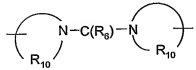


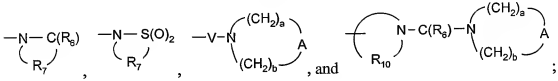
;

Z is selected from the group consisting of a bond, alkylene, alkenylene, and alkynylene;

R_4 is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, arylalkylenyl, aryloxyalkylenyl, alkylarylenyl, heteroaryl, heteroarylalkylenyl,

heteroaryloxyalkylenyl, alkylheteroarylenyl, and heterocyclyl wherein the alkyl, alkenyl, alkynyl, aryl, arylalkylenyl, aryloxyalkylenyl, alkylarylenyl, heteroaryl, heteroarylalkylenyl, heteroaryloxyalkylenyl, alkylheteroarylenyl, and heterocyclyl groups can be unsubstituted or substituted by one or more substituents independently selected from the group consisting of alkyl, alkoxy, hydroxyalkyl, haloalkyl, haloalkoxy, halogen, nitro, hydroxy, mercapto, cyano, aryl, aryloxy, arylalkyleneoxy, heteroaryl, heteroaryloxy, heteroarylalkyleneoxy, heterocyclyl, amino, alkylamino, dialkylamino, (dialkylamino)alkyleneoxy, and in the case of alkyl, alkenyl, alkynyl, and heterocyclyl, oxo;

R_5 is selected from the group consisting of:



;

R_6 is selected from the group consisting of =O and =S;

R_7 is C_{2-7} alkylene;

R_8 is selected from the group consisting of hydrogen, alkyl, alkoxyalkylenyl, and arylalkylenyl;

R_9 is selected from the group consisting of hydrogen and alkyl;

R_{10} is C_{3-8} alkylene;

A is selected from the group consisting of -O-, -C(O)-, $-S(O)_{0-2}$-, $-CH_2$-, and $-N(R_4)$-;

Q is selected from the group consisting of a bond, $-C(R_6)$-, $-C(R_6)-C(R_6)$, $-S(O)_2$-, $-C(R_6)-N(R_8)-W$-, $-S(O)_2-N(R_8)$-, $-C(R_6)-O$-, and $-C(R_6)-N(OR_9)$-;

V is selected from the group consisting of $-C(R_6)$-, $-O-C(R_6)$-, $-N(R_8)-C(R_6)$-, and $-S(O)_2$-;

W is selected from the group consisting of a bond, -C(O)-, and $-S(O)_2$-; and

a and b are independently integers from 1 to 6 with the proviso that $a + b$ is ≤ 7;

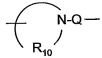
or a pharmaceutically acceptable salt thereof.

6. The compound or salt of claim 3 wherein n is 0.

7. The compound or salt of any one of claims 1 through 6 wherein:

R_1 is selected from the group consisting of alkyl, arylalkylenyl, aryloxyalkylenyl, hydroxyalkyl, fluoroalkyl, heterocyclylalkylenyl which is unsubstituted or substituted by hydroxy, -X-Y-R_4, and -X-R_5, wherein:

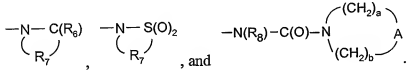
X is alkylene;

Y is selected from the group consisting of -N(R_8)-C(O)-, -N(R_8)-S(O)$_2$-, 

-N(R_8)-C(O)-N(R_8)-, -S(O)$_2$-, and ;

R_4 is selected from the group consisting of alkyl, aryl, and heteroaryl; and

R_5 is selected from the group consisting of:



, , , and .

8. The compound or salt of claim 7 wherein R_1 is selected from the group consisting of alkyl, arylalkylenyl, aryloxyalkylenyl, hydroxyalkyl, -X-Y-R_4, and -X-R_5.

9. The compound or salt of claim 8 wherein R_1 is selected from the group consisting of alkyl and hydroxyalkyl.

10. The compound or salt of claim 7 wherein R_1 is selected from the group consisting of propyl, 2-methylpropyl, 2-hydroxy-2-methylpropyl, 2,3-dihydroxypropyl, 2-methyl-2-[(methylsulfonyl)amino]propyl, 4-[(methylsulfonyl)amino]butyl, 4-[(morpholin-4-ylcarbonyl)amino]butyl, (1-hydroxycyclopentyl)methyl, (1-hydroxycyclobutyl)methyl, 2-fluoro-2-methylpropyl, tetrahydro-2*H*-pyran-4-ylmethyl, and 4-hydroxytetrahydro-2*H*-pyran-4-ylmethyl.

11. The compound or salt of claim 10 wherein R_1 is selected from the group consisting of propyl, 2-methylpropyl, 2-hydroxy-2-methylpropyl, 2,3-dihydroxypropyl, 2-methyl-2-[(methylsulfonyl)amino]propyl, 4-[(methylsulfonyl)amino]butyl, and 2-fluoro-2-methylpropyl.

12. The compound or salt of any one of claims 1 through 11 wherein R_2 is selected from the group consisting of hydrogen, alkyl, alkoxyalkylenyl, and hydroxyalkylenyl.

13. The compound or salt of claim 12 wherein R_2 is selected from the group consisting of hydrogen, alkyl, and alkoxyalkylenyl.

14. The compound or salt of claim 12 wherein R_2 is selected from the group consisting of hydrogen, methyl, ethyl, propyl, butyl, methoxymethyl, ethoxymethyl, 2-methoxyethyl, hydroxymethyl, and 2-hydroxyethyl.

15. The compound or salt of claim 14 wherein R_2 is selected from the group consisting of hydrogen, methyl, ethyl, propyl, butyl, methoxymethyl, ethoxymethyl, and 2-methoxyethyl.

16. The compound or salt of claim 14 wherein R_2 is selected from the group consisting of methyl, ethyl, propyl, methoxymethyl, ethoxymethyl, 2-methoxyethyl, hydroxymethyl, and 2-hydroxyethyl.

17. The compound or salt of any one of claims 1 through 16 wherein Z is selected from the group consisting of a bond, methylene, and ethylene.

18. The compound or salt of claim 17 wherein Z is a bond.

19. The compound or salt of any one of claims 1 through 18 wherein R_3 is -Z-Ar.

20. The compound or salt of any one of claims 1 through 16 wherein R_3 is selected from the group consisting of phenyl, pyridyl, pyrrolyl, pyrazolyl, imidazolyl, thienyl, pyrimidinyl, furyl, and quinolinyl; each of which can be unsubstituted or can be substituted by one or more substituents selected from the group consisting of halogen, alkyl, alkenyl, hydroxy, hydroxyalkyl, alkoxy, amino, aminoalkyl, cyano, methylenedioxy, arylalkyleneoxy, carboxy, haloalkyl, and dialkylamino.

21. The compound or salt of claim 20 wherein R_3 is selected from the group consisting of phenyl, pyridyl, pyrrolyl, pyrazolyl, imidazolyl, thienyl, pyrimidinyl, and furyl; each of which can be unsubstituted or can be substituted by one or more substituents selected from the group consisting of halogen, alkyl, alkenyl, hydroxy, hydroxyalkyl, alkoxy, amino, aminoalkyl, and cyano.

22. The compound or salt of any one of claims 1 through 16 wherein R_3 is selected from the group consisting of pyridin-3-yl, pyridin-4-yl, 5-(hydroxymethyl)pyridin-3-yl, 2-ethoxyphenyl, 3-(morpholin-4-ylcarbonyl)phenyl, 3-[(isopropylamino)carbonyl]phenyl, 3-[(propylamino)carbonyl]phenyl, phenyl, 3-(hydroxymethyl)phenyl, 6-fluoropyridin-3-yl, 4-chlorophenyl, 2-hydroxyphenyl, 2-isopropoxyphenyl, 3,4-difluorophenyl, 3-[(methylsulfonyl)amino]phenyl, 4-[(methylsulfonyl)amino]phenyl, and 3-(aminocarbonyl)phenyl.

23. The compound or salt of claim 22 wherein R_3 is selected from the group consisting of pyridin-3-yl, pyridin-4-yl, 5-(hydroxymethyl)pyridin-3-yl, 2-ethoxyphenyl, and 3-(morpholin-4-ylcarbonyl)phenyl.

24. The compound or salt of claim 22 wherein R_3 is selected from the group consisting of pyridin-3-yl, 3-[(isopropylamino)carbonyl]phenyl, 3-[(propylamino)carbonyl]phenyl, 3-(morpholin-4-ylcarbonyl)phenyl, 3-[(methylsulfonyl)amino]phenyl, 5-(hydroxymethyl)pyridin-3-yl, and 6-fluoropyridin-3-yl.

25. The compound or salt of any one of claims 1 through 18 wherein R_3 is -Z-Ar'-Y-R_4, -Z-Ar'-X-Y-R_4, -Z-Ar'-R_5, or -Z-Ar'-X-R_5.

26. The compound or salt of claim 25 wherein:

Ar' is phenylene or pyridylene;

Y in -Z-Ar'-Y-R_4 or -Z-Ar'-X-Y-R_4 is selected from the group consisting of:

$-S(O)_{0-2}-$,

$-S(O)_2-N(R_8)-$,

-C(O)-,

-$N(R_8)$-Q-,

-$C(R_6)$-$N(R_8)$-,

-C(O)-O-, and

-C(O)-$N(OCH_3)$-;

wherein:

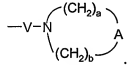
Q is selected from the group consisting of a bond, -C(O)-, -C(O)-O-, -C(O)-N(H)-, and -$S(O)_2$-; and

R_8 is selected from the group consisting of hydrogen, C_{1-4} alkyl, and alkoxyalkylenyl;

X in -Z-Ar'-X-Y-R_4 or -Z-Ar'-X-R_5 is C_{1-4} alkylene;

R_4 in -Z-Ar'-Y-R_4 or -Z-Ar'-X-Y-R_4 is selected from the group consisting of alkyl, haloalkyl, aryl, arylalkylenyl, heteroarylalkylenyl, heteroaryl, alkylheteroarylenyl, and heterocyclyl, with the proviso that R_4 may also be hydrogen when Y is -C(O)-O-, -C(O)-$N(OCH_3)$-, or -$N(R_8)$-; and

R_5 in -Z-Ar'-R_5 or -Z-Ar'-X-R_5 is



27. The compound or salt of claim 25 wherein R_3 is -Z-Ar'-Y-R_4, -Z-Ar'-X-Y-R_4, or -Z-Ar'-R_5.

28. The compound or salt of claim 27 wherein:

Ar' is phenylene or pyridylene;

Y in -Z-Ar'-Y-R_4 or -Z-Ar'-X-Y-R_4 is selected from the group consisting of:

-$S(O)_{0-2}$-,

-C(O)-,

-$N(R_8)$-Q-, and

-$C(R_6)$-$N(R_8)$-;

wherein:

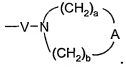
Q is selected from the group consisting of a bond, -C(O)-, -C(O)-O-, and -$S(O)_2$-; and

R_8 is selected from the group consisting of hydrogen, C_{1-4} alkyl, and alkoxyalkylenyl;

X in -Z-Ar'-X-Y-R_4 is C_{1-4} alkylene;

R_4 in -Z-Ar'-Y-R_4 or -Z-Ar'-X-Y-R_4 is selected from the group consisting of alkyl, aryl, arylalkylenyl, heteroarylalkylenyl, heteroaryl, and heterocyclyl; and

R_5 in -Z-Ar'-R_5 is



29. A pharmaceutical composition comprising a therapeutically effective amount of a compound or salt of any one of claims 1 through 28 in combination with a pharmaceutically acceptable carrier.

30. A method of inducing cytokine biosynthesis in an animal comprising administering an effective amount of a compound or salt of any one of claims 1 through 28 or a composition of claim 29 to the animal.

31. A method of treating a viral disease in an animal in need thereof comprising administering a therapeutically effective amount of a compound or salt of any one of claims 1 through 28 or a composition of claim 29 to the animal.

32. A method of treating a neoplastic disease in an animal in need thereof comprising administering a therapeutically effective amount of a compound or salt of any one of claims 1 through 28 or a composition of claim 29 to the animal.